L2 ANSWER 72 OF 1982 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:249660 BIOSIS
DOCUMENT NUMBER: PREV200000249660
TITLE: Complications of **carbon monoxide** poisoning.
AUTHOR(S): Al-Moamary, Mohamed S. (1); Al-Shammary, Afaf S.; Al-Shimemeri, Abdullah A.; Ali, Mir M.; Al-Jahdali, Hamdan H.; Awada, Adnan A.
CORPORATE SOURCE: (1) Department of Medicine, King Fahad National Guard Hospital, Riyadh, 11671 Saudi Arabia
SOURCE: Saudi Medical Journal, (April, 2000) Vol. 21, No. 4, pp. 361-363.
ISSN: 0379-5284.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Objective: Acute **carbon monoxide** poisoning is a common problem that occurs during winter and leads to serious complications. Methods: We retrospectively studied 24 consecutive cases admitted with the aim of finding the causes and outcome of acute **carbon monoxide** poisoning. Results: The source of poisoning was charcoal in 71% of patients, motor gasoline in 21%, and other causes in 8%. Immediate complications included altered consciousness level in 54% of patients, metabolic acidosis in 46%, ***pneumonia*** in 42%, cardiac arrhythmia in 29% and rhabdomyolysis in 25%. Late neurological complications occurred in 17% of patients. All the patients received 100% oxygen. Eleven patients (46%) required mechanical ventilation. Ultimately, 19 patients (79%) recovered completely, 4 (17%) had neurological or cardiac disorders, and 1 (4%) died. Conclusion: Immediate and late complications are common in **carbon monoxide** poisoning cases admitted to the hospital especially when they arrive late. Time lapse between exposure and presentation may have a role in predicting the outcome.
CONCEPT CODE: Public Health: Epidemiology - Miscellaneous *37056
Mathematical Biology and Statistical Methods *04500
Social Biology; Human Ecology *05500
Pathology, General and Miscellaneous - General *12502
Pathology, General and Miscellaneous - Diagnostic *12504
Pathology, General and Miscellaneous - Therapy *12512
Toxicology - General; Methods and Experimental *22501
BIOSYSTEMATIC CODE: Hominidae 86215
INDEX TERMS: Major Concepts
Epidemiology (Population Studies); Toxicology
INDEX TERMS: Diseases
carbon monoxide poisoning: causes, complications, outcome, toxicity
INDEX TERMS: Chemicals & Biochemicals
carboxyhemoglobin
INDEX TERMS: Alternate Indexing
Carbon Monoxide Poisoning (MeSH)
GEOGRAPHICAL TERMS: Saudi Arabia (Palearctic region)
ORGANISM: Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata,

	Animalia
ORGANISM:	Organism Name
	human (Hominidae): patient
ORGANISM:	Organism Superterms
	Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L8 ANSWER 346 OF 849 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 119
ACCESSION NUMBER: 81224244 EMBASE
DOCUMENT NUMBER: 1981224244
TITLE: **Carbon monoxide** and exercise tolerance in chronic **bronchitis** and **emphysema**.
AUTHOR: Calverley P.M.A.; Leggett R.J.E.; Flenley D.C.
CORPORATE SOURCE: Roy. Infirm., Edinburgh, United Kingdom
SOURCE: British Medical Journal, (1981) 283/6296 (878-880).
CODEN: BMJOAE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
015 Chest Diseases, Thoracic Surgery and Tuberculosis
006 Internal Medicine
035 Occupational Health and Industrial Medicine
LANGUAGE: English
ABSTRACT:
The effects of **carbon monoxide** on exercise tolerance as assessed by the distance walked in 12 minutes were studied in 15 patients with severe chronic **bronchitis** and **emphysema** (mean forced expiratory volume in one second 0.56 1, mean forced vital capacity 1.54 1). Each subject walked breathing air and oxygen before and after exposure to sufficient **carbon monoxide** to raise their venous carboxyhaemoglobin concentration by 9%. There was a significant reduction in the walking distance when the patients breathed air after exposure to ***carbon*** **monoxide** ($p < 0.01$), and the significant increase in walking distance seen after exercise when breathing oxygen at 2 1/minute via nasal cannulae was abolished if **carbon monoxide** had previously been administered. Thus concentrations of carboxyhaemoglobin frequently found in bronchitic patients who smoke may reduce their tolerance of everyday exercise, possibly by interfering with the transport of oxygen to exercising muscles.

CONTROLLED TERM: Medical Descriptors:
*chronic bronchitis
*exercise
***lung emphysema**
*smoking
lung function test
respiratory system
major clinical study
therapy
blood and hemopoietic system
Drug Descriptors:
***carbon monoxide**
*carboxyhemoglobin
CAS REGISTRY NO.: (**carbon monoxide**) **630-08-0**;
(carboxyhemoglobin) 9061-29-4

L6 ANSWER 513 OF 1541 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:513800 SCISEARCH
THE GENUINE ARTICLE: 447AR
TITLE: **Carbon monoxide** attenuates aero allergen-induced inflammation in mice
AUTHOR: Chapman J T; Otterbein L E; Elias J A; Choi A M K (Reprint)
CORPORATE SOURCE: Univ Pittsburgh, Sch Med, Div Pulm Allergy & Crit Care Med, MUH 628 NW, Pittsburgh, PA 15213 USA (Reprint); Univ Pittsburgh, Sch Med, Div Pulm Allergy & Crit Care Med, Pittsburgh, PA 15213 USA; Yale Univ, Sch Med, Pulm & Crit Care Med Sect, New Haven, CT 06520 USA; Connecticutt Vet Affairs Healthcare Syst, W Haven, CT 06516 USA; Cleveland Clin Fdn, Dept Pulm & Crit Care Med, Cleveland, OH 44195 USA
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR
PHYSIOLOGY, (JUL 2001) Vol. 281, No. 1, pp. L209-L216. Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 1040-0605.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 69
ABSTRACT:

Carbon monoxide (CO) generated by catalysis of heme by heme oxygenase is increased in the exhaled air of asthmatic patients. Based on recent studies demonstrating that **asthma** is an inflammatory disease associated with increased oxidants and that CO confers cytoprotection in oxidant-induced lung injury and inflammation, we sought to better understand the functional role of CO in **asthma** by using an aeroallergen model. Mice were sensitized to ovalbumin, challenged with aerosolized ovalbumin, and maintained in either CO (250 parts/million) or room air for 48 h. The differential effects of CO on bronchoalveolar lavage (BAL) fluid cell types were observed, with a marked attenuation of BAL fluid eosinophils in the CO-treated animals at 24 and 48 h. A marked reduction of the proinflammatory cytokine interleukin-5 was observed in the CO-treated mice, with no significant changes for other proinflammatory cytokines. These differential Effects of CO were also observed with leukotrienes (LTs) and prostaglandins in that CO significantly decreased BAL fluid PGE(2), and LTB4 but exerted negligible effect on thromboxane B-2 or LTC4/D-4/E-4. Our data suggest a putative immunoregulatory role for CO in aeroallergen-induced inflammation in mice.

CATEGORY: PHYSIOLOGY; RESPIRATORY SYSTEM
SUPPLEMENTARY TERM: heme oxygenase; **asthma**; eosinophils; ovalbumin; cytokines
SUPPL. TERM PLUS: HYPEROXIC LUNG INJURY; CYTOKINE MESSENGER-RNA; MURINE MODEL; AIRWAY HYPERRESPONSIVENESS; BRONCHOALVEOLAR LAVAGE; BRONCHIAL HYPERRESPONSIVENESS; EOSINOPHILIC INFLAMMATION; PULMONARY INFLAMMATION; HEME OXYGENASE-1; OXIDATIVE STRESS

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
AZZAWI M	1990	142	1407	AM REV RESPIR DIS
BOUSQUET J	1990	323	1033	NEW ENGL J MED
BRUSSELLE G	1995	12	254	AM J RESP CELL MOL
CIESLEWICZ G	1999	104	301	J CLIN INVEST
COHN L	1998	161	3813	J IMMUNOL
COHN L	1999	190	1309	J EXP MED
CORRY D B	1997	185	1715	J EXP MED
CORRY D B	1996	183	109	J EXP MED
CORRIGAN C J	1990	141	970	AM REV RESPIR DIS
COTT G R	1986	250	C222	AM J PHYSIOL
COYLE A J	1998	28	2640	EUR J IMMUNOL
COYLE A J	1995	181	1229	J EXP MED
DECHATELET L R	1977	50	525	BLOOD
EUM S Y	1995	92	12290	P NATL ACAD SCI USA
FOSTER P S	1996	183	195	J EXP MED
GARLISI C G	1997	17	642	AM J RESP CELL MOL
GARTY B Z	1998	81	563	ANN ALLERG ASTHMA IM
GAUVREAU G M	1999	159	31	AM J RESP CRIT CARE
GAVETT S H	1994	10	587	AM J RESP CELL MOL
GLEICH G J	1989	88	59	INT ARCH ALLER A IMM
HAJAT S	1999	54	597	THORAX
HAMELMANN E	1997	155	819	AM J RESP CRIT CARE
HOGAN S P	1997	99	1329	J CLIN INVEST
HOLM B A	1985	59	1402	J APPL PHYSIOL
HOLM B A	1988	65	2672	J APPL PHYSIOL
HORVATH I	1998	53	668	THORAX
HUANG J	1998	72	141	ARCH TOXICOL
HUANG S K	1995	155	2688	J IMMUNOL
INMAN M D	1999	21	473	AM J RESP CELL MOL
JACKSON R M	1985	88	900	CHEST
JAGELS M A	1999	21	418	AM J RESP CELL MOL
JENKINSON S G	1993	1	504	NEW HORIZONS
JIA Y X	1999	120	141	INT ARCH ALLERGY IMM
JONES R A	1971	19	46	TOXICOL APPL PHARM
KANTEN W E	1983	244	H320	AM J PHYSIOL
KUNG T T	1994	105	83	INT ARCH ALLERGY IMM
LEFORT J	1996	97	788	J ALLERGY CLIN IMMUN
LENFANT C	1990	98	226	CHEST
MASON R J	1982	79	6033	P NATL ACAD SCI USA
MATALON S	1988	14	1021	EXP LUNG RES
MATALON S	1999	61	627	ANNU REV PHYSIOL
MATALON S	1994	76	989	J APPL PHYSIOL
MINOO P	1992	263	L291	AM J PHYSIOL
MINOO P	1991	261	L386	AM J PHYSIOL
MURALI P S	1992	60	1952	INFECT IMMUN
NDISANG J F	1999	43	65	IMMUNOPHARMACOLOGY
OHKAWARA Y	1997	16	510	AM J RESP CELL MOL
OTTERBEIN L E	1999	276	L688	AM J PHYSIOL
OTTERBEIN L E	2000	6	422	NAT MED
PALMER R M J	1980	20	411	PROSTAGLANDINS
PAREDI P	1999	13	48	EUR RESPIR J

PEACOCK C D	1999	104	153	J ALLERGY CLIN IMMUN
PETAJAN J H	1976	33	152	ARCH NEUROL-CHICAGO
PONATH P D	1996	97	604	J CLIN INVEST
RAHMAN I	1996	154	1055	AM J RESP CRIT CARE
ROBINSON D	1993	92	313	J ALLERGY CLIN IMMUN
ROONEY S A	1994	8	957	FASEB J
SCHWARZE J	1999	162	2997	J IMMUNOL
SOARES M P	1998	4	1073	NAT MED
STUPFEL M	1970	174	342	ANN NY ACAD SCI
TOHDA Y	1999	21	541	METHOD FIND EXP CLIN
UNDERWOOD D C	2000	293	281	J PHARMACOL EXP THER
WAGENER F A D T G	1999	291	416	J PHARMACOL EXP THER
WARDLAW A J	1989	84	19	J ALLERGY CLIN IMMUN
WEISS K B	1992	326	862	NEW ENGL J MED
WHITSETT J A	1998	1408	303	BBA-MOL BASIS DIS
WIKENHEISER K A	1992	262	L32	AM J PHYSIOL
ZAYASU K	1997	156	1140	AM J RESP CRIT CARE
ZHU Z	1999	103	779	J CLIN INVEST

L2 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:274797 CAPLUS
DOCUMENT NUMBER: 131:67924
TITLE: **Carbon monoxide** provides protection against hyperoxic **lung** injury
AUTHOR(S): Otterbein, Leo E.; Mantell, Lin L.; Choi, Augustine M. K.
CORPORATE SOURCE: Section of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, 06520, USA
SOURCE: American Journal of Physiology (1999), 276(4, Pt. 1), L688-L694
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-9 (Pharmacology)
ABSTRACT:

Findings in recent years strongly suggest that the stress-inducible gene heme oxygenase (HO)-1 plays an important role in protection against oxidative stress. Although the mechanism(s) by which this protection occurs is poorly understood, we hypothesized that the gaseous mol. **carbon** ***monoxide*** (CO), a major byproduct of heme catalysis by HO-1, may provide protection against oxidative stress. We demonstrate here that animals exposed to a low concn. of CO exhibit a marked tolerance to lethal concns. of ***hyperoxia*** in vivo. This increased survival was assocd. with highly significant attenuation of **hyperoxia**-induced **lung** injury as assessed by the vol. of pleural effusion, protein accumulation in the airways, and histol. anal. The lungs were completely devoid of **lung** airway and parenchymal inflammation, fibrin deposition, and pulmonary edema in rats exposed to **hyperoxia** in the presence of a low concn. of CO. Furthermore, exogenous CO completely protected against **hyperoxia** -induced **lung** injury in rats in which endogenous HO enzyme activity was inhibited with tin protoporphyrin, a selective inhibitor of HO. Rats exposed to CO also exhibited a marked attenuation of **hyperoxia** -induced neutrophil infiltration into the airways and total **lung** apoptotic index. Taken together, our data demonstrate, for the first time, that CO can be therapeutic against oxidative stress such as **hyperoxia** and highlight possible mechanism(s) by which CO may mediate these protective effects.

SUPPL. TERM: **carbon monoxide** protection hyperoxic **lung** injury
INDEX TERM: Antioxidants
Hyperoxia
(**carbon monoxide** provides protection against hyperoxic **lung** injury)
INDEX TERM: **Lung**, disease
(injury; **carbon monoxide** provides protection against hyperoxic **lung** injury)
INDEX TERM: 9059-22-7
ROLE: BSU (Biological study, unclassified); BIOL (Biological

study)
(1; **carbon monoxide** provides protection against hyperoxic **lung** injury)

INDEX TERM: 7782-44-7, Oxygen, biological studies
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**carbon monoxide** provides protection against hyperoxic **lung** injury)

INDEX TERM: 630-08-0, **Carbon monoxide**, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(**carbon monoxide** provides protection against hyperoxic **lung** injury)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Abraham, N; Proc Natl Acad Sci USA 1995, V92, P6798 CAPLUS
(2) Chance, B; Ann NY Acad Sci 1970, V174, P193 CAPLUS
(3) Choi, A; Am J Respir Cell Mol Biol 1995, V13, P74 CAPLUS
(4) Choi, A; Am J Respir Cell Mol Biol 1996, V15, P9 CAPLUS
(5) Clerch, L; J Clin Invest 1993, V91, P499 CAPLUS
(6) Goda, N; J Clin Invest 1998, V101, P604 CAPLUS
(7) Haldane, J; Biochem J 1927, V21, P1068 CAPLUS
(8) Hartsfield, C; Am J Physiol 273 1997, Lung Cell Mol Physiol 17, PL980
(9) Kazzaz, J; J Biol Chem 1996, V271, P15182 CAPLUS
(10) Keyse, S; Proc Natl Acad Sci USA 1989, V86, P99 CAPLUS
(11) Kharitonov, V; Proc Natl Acad Sci USA 1995, V92, P2568 CAPLUS
(12) Lee, P; Am J Respir Cell Mol Biol 1996, V14, P556 CAPLUS
(13) Lee, P; Proc Natl Acad Sci USA 1996, V93, P10393 CAPLUS
(14) Maines, M; Annu Rev Pharmacol Toxicol 1997, V37, P517 CAPLUS
(15) Marilena, G; Biochem Mol Med 1997, V61, P136 CAPLUS
(16) McCoubrey, W; Eur J Biochem 1997, V247, P725 CAPLUS
(17) Morita, T; J Clin Invest 1995, V96, P2676 CAPLUS
(18) Morita, T; Proc Natl Acad Sci USA 1995, V92, P1475 CAPLUS
(19) Otterbein, L; Am J Physiol 275 (Lung Cell Mol Physiol 19) 1998, PL14 CAPLUS
(20) Otterbein, L; Am J Respir Cell Mol Biol 1995, V13, P595 CAPLUS
(21) Otterbein, L; Am J Respir Crit Care Med 1998, V157, PA56
(22) Poss, K; Proc Natl Acad Sci USA 1997, V94, P10925 CAPLUS
(23) Soares, M; Nat Med 1998, V4, P1073 CAPLUS

(24) Steinberg, K; Am J Respir Crit Care Med 1994, V150, P113 MEDLINE
(25) Taylor, J; Am J Physiol 274 (Lung Cell Mol Physiol 18) 1998, PL582 CAPLUS
(26) Tenhunen, R; J Lab Clin Med 1970, V75, P410 CAPLUS
(27) Verma, A; Science 1993, V259, P381 CAPLUS
(28) Vile, G; J Biol Chem 1994, V268, P14678
(29) Vile, G; Proc Natl Acad Sci USA 1994, V91, P2607 CAPLUS
(30) Willis, D; Nat Med 1996, V2, P87 CAPLUS
(31) Zhuo, M; Science 1993, V260, P1946 CAPLUS

L4 ANSWER 44 OF 343 COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:105096 NLDB
TITLE: BODY'S OWN POISONOUS GAS BLOWS BOTH WAYS WHIFF OF **CARBON MONOXIDE** (CO) SAVED MICE FROM LUNG ISCHEMIA, HINTING AT PUTATIVE CLINICAL USES.
SOURCE: BIOWORLD Today, (9 May 2001) Vol. 12, No. 90.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1011
TEXT:

A do-it-yourself, Kevorkian-inspired individual goes into the garage, shuts the door, shoves one end of a length of garden hose into the car's exhaust pipe, leads the other end into the automobile's interior, hits the starter, and breathes deeply.

In this scenario, the suicidal agent is a colorless, odorless, tasteless gas

- **carbon monoxide** (CO). Depending on its concentration and duration in that garage, death can occur in minutes to a few hours.

But suppose that auto-execution is interrupted if the subject's spouse unexpectedly enters the garage, takes in the scene, quickly opens the doors, shuts off the motor and dials 911. Help arrives in time to rush the wannabe victim to the hospital. What then?

"Depending on the CO levels in the person's blood," said cardiovascular specialist David Pinsky, at Columbia University in New York, "the most effective treatment we have today is hyperbaric oxygen. So the patient is put in under high-pressure, super-high oxygen concentrations, which drives the CO off the blood, off the hemoglobin, and then replaces it with oxygen."

Pinsky is senior author of an article in the May 2001 issue of Nature Medicine, titled "Paradoxical rescue from ischemic lung injury by inhaled ***carbon*** **monoxide** driven by derepression of fibrinolysis." In other words, CO's white hat covers a beneficial clot buster.

"The mechanistic finding in the paper," Pinsky told BioWorld Today, "is that CO, which is known to be made in the body, was thought to be an incidental byproduct of the breakdown of heme molecules. Now, rather, it appears that CO actually has a very important physiological role - to maintain blood flow, and prevent clots from accumulating in vessels that have been injured, either by ischemia or inflammation."

Pinsky explained: "**Carbon monoxide** binds to heme, an iron molecule that's encompassed within hemoglobin. This red blood cell transports oxygen from the lungs to the body's tissues - notably the heart and brain. It's actually the iron in the heme ring that binds oxygen, but can also bind CO. So what happens," he went on, "is that CO displaces and reduces the amount of oxygen delivered to tissues. And that's how CO at elevated levels can be

lethal."

What's Toxic CO Doing In Human Blood?

How then can CO confer benefit? "This iron-containing heme molecule isn't found only in hemoglobin," Pinsky elaborated. "It also occurs in various enzymes of the body, one of which is called guanylate cyclase. That's responsible for making within cells a second messenger - an internal signaling
molecule - called cGMP [guanosine cyclic monophosphate].

"The guanylate cyclase is normally in an inactive state," he continued, "but
as soon as CO binds to the heme within that enzyme, it activates it - turns it
on - and then starts churning out cGMP. Nitric oxide [NO]," Pinsky added, "activates that very same enzyme - so that's how CO is in a sense taking over NO's functions.

"One of the other new links we show in our paper," he observed, "is that by causing formation of cGMP, CO sets in motion a cascade of events that leads to the breakdown of clots. It does so via a cGMP intermediary - plasminogen activator inhibitor. This protein suppresses clot formation or accumulation, and reduces fibrinolysis. So CO-generated cGMP has a number of these beneficial effects, which maintain normal blood vessel function and prevent clots from accumulating, among other things."

The co-authors tested these CO effects in vivo:

"What we did," Pinsky narrated, "was tie off the blood supply to the left lung of a mouse, and left that ligature in place for an hour or an hour and a half. Then we released it so the blood flow came back to the lung. We administered CO by inhalational therapy prior to the ligation. Also - because it was very important if we ever anticipate using CO clinically - we gave it during that ischemic event. We found, surprisingly, that too was quite effective.

"Paradoxically," Pinsky said, "blood oxygen levels following the procedure were higher after CO inhalation then after the same procedure in the absence of that treatment. The overall results were that animals that inhaled the gas exhibited significantly better survival and lung function than those that had the identical surgical procedure, but without the CO gas - and rather were breathing just room air. We also studied knockout mice lacking the normal gene
that makes the CO. We were able to rescue those **carbon
monoxide - minus animals."

Pinsky noted one report in the literature "of a patient who lacked the gene to produce CO under stress conditions. And that patient had a lot of problems - anemia, extreme susceptibility to environmental stress, and all the other pathologies you might predict. I don't think that's a very widespread condition - only one report of a single patient that I'm aware of. But it's something that might be investigated.

"In medicine," Pinsky observed, "we use a lot of toxic molecules for a lot

of things. Most chemotherapeutic agents for instance are highly toxic agents, but if we give them judiciously at the right doses, they can be quite effective under the right circumstances. It wouldn't be the first instance of having something that is toxic at one level prove useful at another level."

Gas Of All Gigs Packs Clinical Potentials

"I think we have to be sanguine - no pun intended," he went on, "about the fact that CO may or may not ultimately be useful. Certainly our studies, which
may be provocative, suggest that we should test further. Ultimately, it may find its way into a clinical use.

"In situations where blood flow is compromised," Pinsky continued, "maybe myocardial infarction, maybe stroke, maybe in organ transplantation, right after implantation when an organ is put in, there can be considerable compromised blood flow. And there might be something such as **sepsis**. These are conditions where there may be a use for CO. When inhaled in very low
doses, it might have some therapeutic value. And that was not previously recognized.

"This is the first time," he concluded, "that a group has shown that CO can protect blood vessels and organs from ischemic injury."

Subscription: $1350.00 per year. Published daily (5 times a week).

CONTROLLED TERM: BIO Biotechnology; BUSN Any type of business

L4 ANSWER 217 OF 343 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 28
ACCESSION NUMBER: 1998:178713 BIOSIS
DOCUMENT NUMBER: PREV199800178713
TITLE: Evidence of increased endogenous **carbon monoxide** production in newborn rat endotoxicosis.
AUTHOR(S): Shi, Yuan; Li, Huaqiang; Pan, Jie; Qin, Shiwen; Yao, Zhongkai; Jiang, Dongbo; Shen, Jigao
CORPORATE SOURCE: Dep. Pediatr., Daping Hosp., Third Military Med. Univ. PLA,
Chongqing 630042 China
SOURCE: Chinese Medical Sciences Journal, (Dec., 1997) Vol. 12, No.
4, pp. 212-215.
ISSN: 1001-9294.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:

Carbon monoxide is thought to serve as a new endogenous mediator in the pathogenesis of **sepsis** and **septic** shock. In newborn rat endotoxicosis, **carbon monoxide** levels in the circulation as well as liver, kidney and lung were found to be significantly increased ($P < 0.05$). Moreover, the elevations of **carbon** ***monoxide*** correlated with enhanced nitric oxide production as indicated by nitrite/nitrate levels ($P<0.05$). Our present data showed for the first time that endogenously produced **carbon monoxide** was increased during the course of shock-like states, which suggested that the role of ***carbon*** **monoxide** in **sepsis** and **septic** shock might worth further study.

CONCEPT CODE: Endocrine System - General *17002
Biochemical Studies - General *10060
Metabolism - General Metabolism; Metabolic Pathways *13002
Digestive System - General; Methods *14001
Cardiovascular System - General; Methods *14501
Urinary System and External Secretions - General; Methods *15501
Respiratory System - General; Methods *16001
Medical and Clinical Microbiology - General; Methods and Techniques *36001
BIOSYSTEMATIC CODE: Muridae 86375
INDEX TERMS: Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Infection
INDEX TERMS: Parts, Structures, & Systems of Organisms
circulation: circulatory system; kidney: excretory system; liver: digestive system; lung: respiratory system
INDEX TERMS: Diseases
endotoxicosis: bacterial disease; **sepsis**: bacterial disease; **septic** shock: bacterial disease
INDEX TERMS: Chemicals & Biochemicals
carbon monoxide: production; nitrate; nitric oxide: production; nitrite

ORGANISM:	Super Taxa Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISM:	Organism Name rat (Muridae): newborn
ORGANISM:	Organism Superterms Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
REGISTRY NUMBER:	630-08-0 (**CARBON MONOXIDE**) 10102-43-9 (NITRIC OXIDE) 14797-65-0 (NITRITE) 14797-55-8 (NITRATE)

L4 ANSWER 220 OF 343 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 30
ACCESSION NUMBER: 97247428 EMBASE
DOCUMENT NUMBER: 1997247428
TITLE: Heine oxygenase-dependent **carbon monoxide** production is a hepatic adaptive response to **sepsis**.
AUTHOR: Downard P.J.; Wilson M.A.; Spain D.A.; Matheson P.J.; Siow Y.; Garrison R.N.
CORPORATE SOURCE: Dr. R.N. Garrison, Department of Surgery, University of Louisville, Louisville, KY 40292, United States
SOURCE: Journal of Surgical Research, (1997) 71/1 (7-12).
Refs: 19
ISSN: 0022-4804 CODEN: JSGRA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
009 Surgery
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The hemodynamic effects of **sepsis** have been attributed in part to increased nitric oxide (NO) production and activation of guanylate cyclase, resulting in increased cGMP and relaxation of vascular smooth muscle. Heme oxygenase-1 (HO-1), a heat shock protein, has been shown to increase intracellular cGMP levels by formation of **carbon monoxide** (CO). We hypothesized that HO may be an important mediator of the hepatic response to infection. Male Swiss Webster mice underwent standard cecal ligation and puncture (CLP, 18 gauge 2X) or sham operation, and received either normal saline (NS) or Zn protoporphyrin IX (ZN PP IX), a competitive HO inhibitor (n = 6-8/group). Hepatic tissue samples were collected at 3, 6, 12, and 24 hr from separate mice. Serum was collected at 3 and 24 hr. A semiquantitative reverse transcriptase polymerase chain reaction method was used to measure HO-1 mRNA levels. Hepatic cGMP levels were measured by ELISA. Groups were repeated (n = 10/group) to assess mortality. Serum was collected at 3 and 24 hr to measure serum aspartate aminotransferase (AST) levels. HO-1 mRNA expression increased significantly by 3 hr after CLP and with HO inhibition alone ($P < 0.05$ vs sham + NS). HO-1 mRNA remained elevated through 24 hr. CLP animals with HO inhibition showed a significant reduction of hepatic cGMP following CLP compared with CLP + saline at 24 hr ($P < 0.05$). Mortality was significantly increased in the CLP + ZN PP group at 24 hr ($P < 0.05$ CLP NS vs CLP ZN PP). CLP caused a marked increase in AST activity, which was increased further with HO inhibition. HO1 mRNA expression was induced by CLP. AST levels following CLP were markedly increased with HO inhibition. HO-1 function appeared to contribute to elevation of hepatic cGMP during peritonitis and may be an important hepatic adaptive response to infection.

CONTROLLED TERM: Medical Descriptors:
*bacterial peritonitis: ET, etiology
***sepsis: ET, etiology**
adaptation

animal experiment
animal model
animal tissue
article
controlled study
hemodynamics
liver function
male
mouse
nonhuman
priority journal
vascular smooth muscle
Drug Descriptors:
***carbon monoxide: EC, endogenous compound**
*heme oxygenase: EC, endogenous compound
aspartate aminotransferase: EC, endogenous compound

CAS REGISTRY NO.: (**carbon monoxide**) 630-08-0; (heme oxygenase) 9059-22-7; (aspartate aminotransferase) 9000-97-9

L4 ANSWER 316 OF 343 FEDRIP COPYRIGHT 2002 NTIS
ACCESSION NUMBER: 2002:46559 FEDRIP
NUMBER OF REPORT: VA 108058
NUMBER OF CONTRACT: 0019, 603
RESEARCH TITLE: Heme Oxygenase Production During Surgical Peritonitis
STAFF: Principal Investigator: Garrison, Richard N., M.D.
PERFORMING ORGN: Department of Veterans Affairs, Medical Center, Louisville, KY
SUPPORTING ORGN: Supported By: Department of Veterans Affairs, Research and Development (15), 810 Vermont Ave. N.W.,
Washington, D.C., 20420, United States of America
PROJECT START DATE: Mar 1, 1996
FILE SEGMENT: Department of Veterans Affairs
SUMMARY: **SEPSIS**; PERITONITIS; HEME OXYGENASE
OBJECTIVES: Nitric oxide (NO) and **carbon monoxide** (CO) control severa l physiological mechanisms through the second messenger cyclic GMP (cGMP), and show increased production during shock and **septic** states. We have demonstrated that blockade of heme oxygenase-dependant CO production exacerbates hepatic injury during **sepsis**. However the interplay between CO and NO regulation has not been investigated in this model. We hypothesized that the NO and CO generating systems are independently regulated during **sepsis** RESEARCH PLAN: Animals were randomly assigned to experimental groups. Differences among groups were determined by analysis of variance (ANOVA) and by Tukey-Kramer HSD with a priori $p<0.05$ for significance. METHODOLOGY: Male Swiss Webster mice underwent standard cecal ligatio n and puncture (CLP, 18 Gauge 2X) or sham operation, and received either normal saline, NS) or Tin protoporphyrin IX (SnPPIX), a competitive HO inhibitor (n=5-6/group). Ileum tissue and serum samples were collected at 3 and 24 hrs. A semi-quantitative reverse transcriptase
PCR method was used to measure inducible heme oxygenase (HO-1) and inducible NO synthase (iNOS) mRNA production. Serum NO metabolites were measured using a fluorescence assay. FINDINGS: Ileal HO-1i and iNOS mRNA production increased significantl y in CLP+NS and CLP+SnPPIX groups at 24 hrs. versus Shams with saline alone ($p<0.05$) and also in Shams treated with SnPPIX ($p<0.05$). Serum NO metabolites increased significantly in CLP+NS and CLP + SnPPIX groups versus Sham +NS ($p<0.05$). These data indicate blockade of the CO producing heme oxygenase system induces both HO-1 and iNOS mRNA expression in Sham animals, but serum NO metabolite levels are not altered. CLP induced significant levels of both messages, and also increased serum NO metabolites.

These findings were not altered by HO inhibition. Although NO and CO appear to share transcriptional regulation, inhibition of heme oxygenase did not affect systemic metabolites of nitric oxide

synthase.

This study formed the basis for a Merit Review application, which is in its first year of funding. This study remained open pending final review of the manuscripts, in anticipation of possible reviewer requests for additional data. All manuscripts are

now

in print, and this is the final abstract for this proposal. CLINICAL RELATIONSHIPS: We and others

have

previously demonstrated th at the heme oxygenase enzyme system plays a protective role in animal models of **sepsis** and trauma via either the generation of minute amounts of **carbon monoxide**, the breakdown of heme, or both actions. Additionally, it has been demonstrated that significant interregulation between the nitric oxide synthase and the heme oxygenase systems exist. These two systems are involved in many physiological and pathophysiological processes, but the details of their interregulation and its significance are still not clearly understood. Further elucidation of these interregulatory mechanisms may provide new

directions

for the development of appropriate treatments for **sepsis** and traumatic injuries in humans.

SUBJECT INDEX TERM: **SEPSIS**; PERITONITIS; HEME OXYGENASE

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L6 ANSWER 273 OF 1541 Elsevier BIOBASE COPYRIGHT 2002 Elsevier Science B.V.

ACCESSION NUMBER: 1998191307 Elsevier BIOBASE

TITLE: Raised levels of exhaled **carbon monoxide** are associated with an increased expression of heme oxygenase-1 in airway macrophages in **asthma**: A new marker of oxidative stress

AUTHOR: Horvath I.; Donnelly L.E.; Kiss A.; Paredi P.; Kharitonov S.A.; Barnes P.J.

CORPORATE SOURCE: Prof. P.J. Barnes, Department of Thoracic Medicine, National Heart and Lung Institute, Imperial Colleges, Dovehouse Streets, London SW3 6LY, United Kingdom.

SOURCE: Thorax, (1998), 53/8 (668-672), 19 reference(s)
CODEN: THORA7 ISSN: 0040-6376

DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Background - Chronic inflammatory diseases are associated with an increased production of oxidants. Induction of a stress protein, heme oxygenase (HO) HO-1, is a cytoprotective mechanism against oxidative cellular injury. HO-1 catabolises heme to bilirubin, free iron, and **carbon monoxide** (GO). Methods - Exhaled GO and sputum bilirubin levels were measured and HO- 1 protein expression in airway macrophages was determined by Western blotting in asthmatic patients as levels of oxidants are raised in **asthma** and may induce HO-1. Results - Exhaled GO was significantly increased in 37 non- steroid treated asthmatic patients compared with 37 healthy subjects (5.8 (95% CI 5.20 to 6.39) ppm vs 2.9 (2.51 to 3.28) ppm; p<0.0001) but was similar to normal in 25 patients who received corticosteroids (3.3 (95% CI 2.92 to 3.67) ppm; p>0.05). In non-treated asthmatic patients more HO-1 protein was expressed in airway macrophages than in normal subjects. Bilirubin levels in induced sputum were also higher than in normal subjects. Inhalation of heroin, a substrate for HO, significantly increased exhaled CO from 3.8 (95% CI 2.80 to 4.87) ppm to 6.7 (95% CI 4.95 to 8.38 CI) ppm (p<0.05) with a concomitant decrease in exhaled nitric oxide levels, suggesting an interaction between the two systems. Conclusions - Increased exhaled CO levels and HO-1 expression may reflect induction of HO-1 which may be inhibited by steroids. Measurement of exhaled CO, an index of HO activity in non-smoking subjects, may therefore be clinically useful in the detection and management of **asthma** and possibly other chronic inflammatory lung disorders.

CLASSIFICATION CODE: 86.8.1.3 IMMUNOLOGY AND INFECTIOUS DISEASES: IMMUNE RESPONSE DISORDERS: Acute Inflammation, Immediate Hypersensitivity, Anaphylaxis: Human studies
86.3.7.2 IMMUNOLOGY AND INFECTIOUS DISEASES: CELLS OF THE IMMUNE SYSTEM: Macrophages, Mononuclear Phagocytes: Biochemistry

SUPPLEMENTARY TERM: Heme oxygenase-1; **Asthma**; Exhaled **carbon monoxide**; Inflammation

L14 ANSWER 885 OF 6227 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 214
ACCESSION NUMBER: 1975:133653 CAPLUS
DOCUMENT NUMBER: 82:133653
TITLE: Effect of **carbon monoxide** on cellular respiration and glycolysis in Ehrlich **cancer** cells
AUTHOR(S): Zakhvatkin, S. V.
CORPORATE SOURCE: L'vov. Med. Inst., Lvov, USSR
SOURCE: Sovrem. Probl. Biokhim. Dykhaniya Klin., Mater. Vses. Konf., 2nd (1972), Meeting Date 1971, Volume 1, 341-3. Editor(s): Usol'tseva, V. A. Ivanov. Gos. Med. Inst.: Ivanovo, USSR.
CODEN: 29LJA7
DOCUMENT TYPE: Conference
LANGUAGE: Russian
CLASSIFICATION: 4-3 (Toxicology)
ABSTRACT:
Exposure of ascites Ehrlich **cancer** cells to CO [**630-08-0**] with an addn. of 2% O for 1 hr significantly decreased the rate of O uptake and increased the rate of glycolysis. The changes persisted after the removal of CO. A decrease in the viability of cells was also obsd. The toxic effects of CO may be due to the accumulation of lactic acid in the cells.

SUPPL. TERM: respiration **neoplasm carbon monoxide**; **carbon monoxide** respiration tumor cell; glycolysis tumor cell **carbon monoxide**
INDEX TERM: Animal respiration
Glycolysis
(by **neoplasms**, **carbon monoxide** effect on)
INDEX TERM: **Neoplasm**, metabolism
(respiration by, **carbon monoxide** effect on)
INDEX TERM: **630-08-0**, biological studies
ROLE: BIOL (Biological study)
(**neoplasm** respiration response to)

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L14 ANSWER 911 OF 6227 NIOSHTIC
ACCESSION NUMBER: 1997:18892 NIOSHTIC
DOCUMENT NUMBER: NIOSH-00026382
TITLE: **Cancer** of Skin and Increase in Incidence of Primary Tumours of Lung in Mice Exposed to Dust Obtained from Tarred Roads
AUTHOR(S): Campbell, J. A.
SOURCE: British Journal of Experimental Pathology, Vol. 15, No. 5, pages 287-294, 9 references
PUBLICATION DATE: Oct 1934
LANGUAGE: ENGLISH
ABSTRACT:
Mice exposed repeatedly to dust from tarred roads, containing 2% tar, developed more **cancer** of the skin and primary adenoma of the lung than did control animals. The lungs of the dusted mice contained large amounts of dust. The effect of dusting was retarded by the inhalation of **carbon** ***monoxide*** . Dust exposure of mice was much greater than that normally occurring in man.

CONTROLLED TERM: Lloyd; Carcinogenesis; Dust inhalation; Lung adenoma; Lung **cancer**; Respiratory disorders; Skin disorders; Air contamination; 630080

L14 ANSWER 913 OF 6227 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1934:17114 CAPLUS
DOCUMENT NUMBER: 28:17114
ORIGINAL REFERENCE NO.: 28:2064i,2065a
TITLE: **Cancer** chemotherapy. XI. The effect of **carbon monoxide**, hydrocyanic acid and pituitrin upon tumor growth
AUTHOR(S): Maxwell, L. C.; Bischoff, Fritz; Ullman, Henry, Jr.
SOURCE: J. Pharmacol. (1933), 49, 270-82
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
CLASSIFICATION: 11H (Biological Chemistry: Pharmacology)
ABSTRACT:
Exposure of animals bearing transplantable tumors to CO and to HCN resulted in a decrease in the rate of tumor growth, whereas sublethal doses of pituitrin did not. There was no significant change of lipoid and cholesterol values of the tumors or of lipoid and glycogen values of other tissues accompanying such treatment.

L14 ANSWER 914 OF 6227 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1933:27362 CAPLUS
DOCUMENT NUMBER: 27:27362
ORIGINAL REFERENCE NO.: 27:2491i,2492a
TITLE: The influence of breathing **carbon monoxide** and oxygen at high percentages for prolonged periods of time upon development of tar **cancer** in mice
AUTHOR(S): Campbell, J. Argyll
SOURCE: J. Path. Bact. (1933), 36, 243-8
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
CLASSIFICATION: 11G (Biological Chemistry: Pathology)
ABSTRACT:
CO (0.24%) breathed for 1/3 of the life retards but does not prevent development of tar **cancer** in mice. There is no evidence that the recently reported increase in human **cancer** is connected with the presence of CO in the air of garages, streets, etc. Breathing 60% O had no effect on the development of tar **cancer**.

L11 ANSWER 285 OF 838 HSDB COPYRIGHT 2002 NLM
CAS Registry No. (RN): **630-08-0** HSDB
HSDB Number (HSN): 903
Chemical Name (CN): **CARBON MONOXIDE**
Last Rev. Date (RDAT): Jan. 18, 2002
RTECS Number (RTN): NIOSH-FG3500000
Molecular Formula (MF): C O **PEER REVIEWED**
Molecular Weight (MW): 28.01
Character Count (CHC): 167692

Chemical Name (CN): **CARBON MONOXIDE**
Synonyms (CN): CARBONE (OXYDE DE) (FRENCH) **PEER REVIEWED**; CARBONIC OXIDE **PEER REVIEWED**; CARBONIO (OSSIDO DI) (ITALIAN) **PEER REVIEWED**; **CARBON MONOXIDE** (DOT) **PEER REVIEWED**; **CARBON OXIDE** (CO) **PEER REVIEWED**; FLUE GAS **PEER REVIEWED**; KOHLENMONOXID (GERMAN) **PEER REVIEWED**; KOOLMONOXYDE (DUTCH) **PEER REVIEWED**; OXYDE DE CARBONE (FRENCH) **PEER REVIEWED**; WEGLA TLENEK (POLISH) **PEER REVIEWED**
Shipping Name/No. (CN): IMO 2.3 **Carbon monoxide**; UN 1016 **Carbon monoxide**
STCC No. (CN): 49 201 90 **Carbon monoxide**
Manufacture/Use Information

Application (APP):
UNISOLATED COMPONENT OF GASEOUS FUELS-EG, WATER GAS; CHEM INT FOR PHOSGENE, METHANOL, ACETIC ACID, ACRYLIC ACID, SYNTHETIC FUELS (NON-U.S. USE), DIMETHYLFORMAMIDE, OXO ALCOHOLS VIA ALDEHYDES (EG, BUTYL ALCOHOL), METHYL FORMATE, ALKYL CARBONATES & SILICON CARBIDE FIBERS; COMONOMER IN ETHYLENE-**CARBON MONOXIDE** COPOLYMER;REDUCING AGENT IN IRON ORE PROCESSING; PURIFICATION AGENT FOR NICKEL VIA NICKEL CARBONYL; CHEM INT FOR OTHER METAL CARBONYLS-EG, TUNGSTEN CARBONYL; CHEM INT FOR ETHYLENE GLYCOL (FORMER USE) **PEER REVIEWED** [SRI]

Manufacture/Use Information

Application (APP):
Carbon monoxide is increasingly being used on a very large scale for the production of chemical intermediates. It is used in the production of syngas which can be used in the synthesis of ammonia. It is used for the synthesis of commodity chemicals and fuels by using syngas as an alternative to petroleum based feedstocks. It is a reducing agent in blast furnaces; production of phosgene; purification of metals; production of acetic acid (consumes more than 500 kt/a), formic acid, methyl formate, N,N-dimethylformamide, acrylic acid, and propanoic acid. A large variety ofchemicals, ranging from saturated hydrocarbons to oxygenated compounds (i.e. methanol), are produced using syngas as a feedstock. **PEER REVIEWED** [Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial

Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA5 211]

Manufacture/Use Information

U.S. Exports (EXPT):
(1984) 1.14E+13 g /Carbon Dioxide, Nitrous Oxide, and **Carbon Monoxide**/ **PEER REVIEWED** [BUREAU OF THE CENSUS. U.S. EXPORTS, SCHEDULE E, 1984 p.2-94]

Physical and Chemical Properties

Other Properties (OCPP):
Burns in air with bright blue flame; top pressure: 1500 psi; heat capacity @ 20 deg C: 6.95 Cal/mole/deg C; heat value/cu m: 3033 kcal; heat of formation: -26.39 Kcal/mol; above 800 deg c equil reaction favors **carbon monoxide** formation; decomp the catalyzer hopcalite (a mixture of the oxides of manganese and copper) @room temp, as does palladium on silica gel **PEER REVIEWED** [Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989.275]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Health: TOXIC; may be fatal if inhaled or absorbed through skin. Contact with gas or liquefied gas may cause burns, severe injury and/or frostbite.
Fire will produce irritating, corrosive and/or toxic gases. Runoff from fire control may cause pollution. /**Carbon monoxide;** **Carbon monoxide,** compressed; **Carbon monoxide** and hydrogen mixture; **carbon monoxide** and hydrogen mixture, compressed/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-119]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Fire or explosion: Flammable; may be ignited by heat, sparks orflames. May form explosive mixtures with air. Some may polymerize (P) explosively when heated or involved in a fire. Vapors from liquefied gas are initially heavier than air and spread along ground. Vapors may travel to source of ignition and flash back. Some of these materials may react violently with water. Containers may explode when heated. Ruptured cylinders may rocket. Runoff may create fire or explosion hazard. /**Carbon monoxide; Carbon monoxide,** compressed; **Carbon monoxide** and hydrogen mixture; **carbon monoxide** and hydrogen mixture, compressed/ **QC REVIEWED** [U.S.

Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-119]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Public safety: CALL Emergency Response Telephone Number on Shipping Paper first. If Shipping Paper not available or no answer, refer to appropriate telephone number listed on the inside back cover. Isolate spill or leak area immediately for at least 100 to 200 meters (330 to 660 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Many gases are heavier than airand will spread along ground and collect in low or confined areas (sewers, basements, tanks). Keep out of low areas. Ventilate closed spaces before entering. /**Carbon monoxide; Carbon monoxide,** compressed; **Carbon monoxide** and hydrogen mixture; **carbon monoxide** and hydrogen mixture, compressed/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-119]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Wear chemical protective clothing which is specifically recommended by the manufacturer. It may provide little or no thermal protection. Structural firefighters' protective clothing is recommended for fire situations ONLY; it is noteffective in spill situations. / **Carbon monoxide; Carbon monoxide,** compressed; **Carbon monoxide** and hydrogen mixture; **carbon monoxide** and hydrogen mixture, compressed/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-119]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Evacuation: Spill: See the Table of Initial Isolation and Protective Action
Distances for highlighted substances. For non-highlighted substances, increase, in the downwind direction, as necessary, the isolation distance shown under "PUBLIC SAFETY". Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 1600 meters (1 mile) in all directions;

also, consider initial evacuation for 1600 meters (1 mile) in all directions. /Carbonmonoxide; **Carbon monoxide,** compressed; **Carbon monoxide** and hydrogen mixture; **carbon monoxide** and hydrogen mixture, compressed/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-119]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Fire: DO NOT EXTINGUISH A LEAKING GAS FIRE UNLESS LEAK CAN BE STOPPED. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. Large fires: Water spray, fog or alcohol-resistant foam. FOR CHLOROSILANES, DO NOT USE WATER; use AFFF alcohol-resistant medium expansion foam. Move containers from fire area ifyou can do it without risk. Damaged cylinders should be handledonly by specialists. Fire involving tanks: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well afterfire is out. Do not direct water at source of leak or safety devices; icing may occur. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from the ends of tanks. /**Carbon monoxide;** **Carbon monoxide,** compressed; **Carbon monoxide** and hydrogen mixture; **carbon monoxide** and hydrogen mixture, compressed/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-119]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used whenhandling the product must be grounded. Fully encapsulating, vapor protective clothing should be worn for spills and leaks with no fire. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Do not direct water at spill orsource of leak. Use water spray to reduce vapors or divert vapor cloud drift. FOR CHLOROSILANES, use AFFF alcohol-resistant medium expansion foam to reduce vapors. If possible, turn leaking containers so that gas escapes rather than liquid. Prevent entry into waterways, sewers, basements or confined areas. Isolate area until gas has dispersed. /**Carbon monoxide; Carbon monoxide,** compressed; **Carbon monoxide** and hydrogen mixture; **carbon monoxide** and hydrogen

mixture, compressed/ **QC REVIEWED** [U.S. Department of Transportation.
1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-119]

Safety and Handling

DOT Emergency Guidelines (DOTG):
First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Do not use mouth-to-mouth method if victim ingested or inhaled the substance; induce artificial respiration with the aid of a pocketmask equipped with a one-way valve or other proper respiratory medical device. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. In case of contact with liquefiedgas, thaw frosted parts with lukewarm water. Keep victim warm and quiet. Keep victim under observation. Effects of contact or inhalation may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves. /**Carbon monoxide; Carbon monoxide,** compressed; Carbonmonoxide and hydrogen mixture; **carbon monoxide** and hydrogen mixture, compressed/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-119]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Health: TOXIC; Extremely hazardous. Inhalation extremely dangerous; may be fatal. Contact with gas or liquefied gas may cause burns, severe injury and/or frostbite. Odorless, will not be detected by sense of smell. / **Carbon monoxide,** refrigerated liquid (cryogenic liquid)/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-168]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Fire or explosion: EXTREMELY FLAMMABLE. May be ignited by heat,sparks or flames. Flame may be invisible. Vapors may travel to source of ignition

and flash back. Containers may explode when heated. Vapor explosion and poison hazard indoors, outdoors or insewers. Vapors from liquefied gas are initially heavier than air and spread along ground. Vapors may travel to source of ignition and flash back. Runoff may create fire or explosion hazard. /**Carbon monoxide,** refrigerated liquid (cryogenic liquid)/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-168]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Public safety: CALL Emergency Response Telephone Number on Shipping Paper first. If Shipping Paper not available or no answer, refer to appropriate telephone number listed on the inside back cover. Isolate spill or leak area immediately for at least 100 to 200 meters (330 to 660 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Many gases are heavier than airand will spread along ground and collect in low or confined areas (sewers, basements, tanks). Keep out of low areas. Ventilate closed spaces before entering. /**Carbon monoxide,** refrigerated liquid (cryogenic liquid)/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-168]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Wear chemical protective clothing which is specifically recommended by the manufacturer. It may provide little or no thermal protection. Structural firefighters' protective clothing is recommended for fire situations ONLY, it is noteffective in spill situations. Always wear thermal protective clothing when handling refrigerated/cryogenic liquids. /**Carbon monoxide,** refrigerated liquid (cryogenic liquid)/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-168]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Evacuation: Spill: See the Table of Initial Isolation and Protective Action

Distances for highlighted substances. For non-highlighted substances, increase, in the downwind direction, as necessary, the isolation distance shown under "PUBLIC SAFETY". Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters 1//2 mile) in all directions. /**Carbon monoxide**, refrigerated liquid (cryogenic liquid)/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-168]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Fire: DO NOT EXTINGUISH A LEAKING GAS FIRE UNLESS LEAK CAN BE STOPPED. Small fires: Dry chemical, CO2 or water spray. Large fires: Water spray, fog or regular foam. Move containers from fire area if you can do it without risk. Fire involving tanks: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Do not direct water at source of leak or safety devices; icing may occur. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from the ends of tanks. / **Carbon monoxide**, refrigerated liquid (cryogenic liquid)/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-168]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used whenhandling the product must be grounded. Fully encapsulating, vapor protective clothing should be worn for spills and leaks with no fire. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Use water spray to reduce vapors or divert vapor cloud drift. Do not direct water at spill or source of leak. If possible, turn leaking containers so that gas escapes rather than liquid. Prevent entry into waterways, sewers, basements or confined areas. Isolate area until gas has dispersed. / **Carbon monoxide**, refrigerated liquid (cryogenic liquid)/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-168]

Safety and Handling

DOT Emergency Guidelines (DOTG):
First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. In case of contact with liquefied gas, thaw frosted parts with lukewarm water. Keep victim warm and quiet. Keep victim under observation. Effects of contact or inhalation may be delayed. Ensure that medical personnel are aware of the material(s)involved, and take precautions to protect themselves. / **Carbon monoxide**, refrigerated liquid (cryogenic liquid)/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-168]

Safety and Handling

DOT Emergency Guidelines (DOTG):
Initial Isolation and Protective Action Distances: Small Spills(from a small package or small leak from a large package): First, ISOLATE in all Directions 30 meters (100 feet); then, PROTECTpersons Downwind during DAY 0.2 kilometers (0.1 miles) and NIGHT 0.2 kilometers (0.1 miles). LARGE SPILLS (from a large packageor from many small packages): First, ISOLATE in all Directions 95 meters (300 feet); then, PROTECT persons Downwind during DAY 0.2 kilometers (0.1 miles) and NIGHT 0.6 kilometers (0.4 miles)./**Carbon monoxide; Carbon monoxide**, compressed/ **QC REVIEWED** [U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. TABLE]

Safety and Handling

Fire Fighting Hazards (FFH):
Carbon monoxide is the most frequent cause of immediate fire deaths, and **carbon monoxide** poisoning should be suspected in everyfire victim. **Carbon monoxide** levels at fires may reach 10%, which can raise carboxyhemoglobin levels in active firefighters without respiratory protection to 75% within 1 minute. **PEER REVIEWED** [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 820]

Safety and Handling

Reaction and Incompatability (REAC):
... Explosion /occurred/ during reduction of iron oxide with **carbon monoxide** /due to/ formation of pentacarbonyliron at temperatures between 0 and 150 deg C. **PEER REVIEWED** [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1136]

Safety and Handling

Reaction and Incompatability (REAC):
Carbon monoxide is exothermically oxidized over silver oxide, and the temperature may attain 300 deg C. **PEER REVIEWED** [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 16]

Safety and Handling

Reaction and Incompatability (REAC):
Synthesis gas (**carbon monoxide** + hydrogen) at 40 bar containinga low level of hydrogen sulfide was to be freed of the latter impurity by adding the theoretical quantity of oxygen and passingthe mixture over a catalyst. Introduction of oxygen (from a supply at 60 bar) via a simple T-piece ... caused development of anintense inverse flame in the locally very high oxygen concentration which burned through the reactor side wall opposite the oxygen inlet and ejected a meter-long flame-jet. **PEER REVIEWED** [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1397]

Safety and Handling

Reaction and Incompatability (REAC):
Several explosions occurred during the preparation /of bis(fluoroformyl) peroxide/, which involves charging **carbon monoxide** into a mixture of fluorine and oxygen. **PEER REVIEWED** [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 215]

Safety and Handling

Reaction and Incompatability (REAC):
Aluminum powder burns when heated in carbon dioxide, and presence of aluminum chloride or aluminum iodide vapor in **carbon monoxide** or carbon dioxide accelerated the reaction to incandescence. **PEER REVIEWED** [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 21]

Safety and Handling

Reaction and Incompatability (REAC):
At temperatures ... above 30 deg C, explosions occurred /with bromine trifluoride and **carbon monoxide**/. **PEER REVIEWED** [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 90]

Safety and Handling

Other Preventative Measures (OPRM):
... Any individual should be protected from exposure to **carbon monoxide** that would result in carboxyhemoglobin levels of 5% forany but transient periods, and that especially susceptible persons ought not to be subjected to concentrations giving carboxyhemoglobin levels exceeding 2.5%. **PEER REVIEWED** [WHO; Environ Health Criteria 13: Carbon Monoxide p.15 (1979)]

Safety and Handling

Disposal Methods (DSM):
Incineration: Remove leaky cylinders to remote area to empty; then return to supplier with label indicating that repairs are needed. The waste **carbon monoxide** can be piped to an approved incinerator or the cylinder can be placed in a pit to burn **carbon monoxide** to carbon dioxide under controlled conditions. **PEER REVIEWED** [United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. 132]

Toxicity

Antidote and Emergency Treatment (ANTR):
The prompt administration of oxygen is critical to maternal andfetal survival. In gestationally appropriate pregnancies, it isreasonable to use indicators of adequate fetal oxygenation central nervous system responsiveness (heart rate and variability), in addition to responses of the mother and her laboratory findings, in adjusting or terminating oxygen therapy. To ensure adequate treatment of the fetus, it has been recommended that the mother receive oxygen therapy for five times as long as it is expected to require to return her **carbon monoxide** concentrations to normal; this is how long it may take for fetal levels to normalize. The maternal carboxyhemoglobin elimination rate can be increased from a half-life of 2 to 3 hours to 3/4 of an hour by breathing 100% oxygen; fetal carboxyhemoglobin half-lives are expected to decease from 6 to 7 hours to 2 to 4 hours by the use of maternal oxygen therapy. The fetal rate of elimination remains slowerthan that of the mother. **PEER REVIEWED** [Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990.,p. 427-8]

Toxicity

Medical Surveillance (MEDS):
The following medical procedures should be made available to each employee who is exposed to **carbon monoxide** at potentially hazardous levels: A complete history and physical examination. ... Examination of the cardiovascular system, the pulmonary system, the blood, and the central nervous system should be stressed. A complete blood count should be performed including a red cell count, a white cell count, a differential count of a stained smear, as well as hemoglobin and hematocrit. ... The aforementioned medical examinations should be repeated on an annual basis, with the exception that a carboxyhemoglobin determination should be performed at any time overexposure is suspected or signs or symptoms of toxicity occur. **PEER REVIEWED** [Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]

Toxicity

Human Toxicity Excerpt (HTXE):
SYMPTOMATOLOGY: 11. DURING CONVALESCENCE A BRONCHOPNEUMONIA MAYDEVELOP BECAUSE OF THE ASPIRATION OF SALIVA OR VOMITUS... 12. MYOCARDIAL INFARCTION, WITH OR WITHOUT CORONARY THROMBOSIS, MAY APPEAR AT ANY TIME UP TO ONE WEEK FOLLOWING AN ACUTE POISONING. 13. AFTER AN UNEVENTFUL CONVALESCENCE, SIGNS OF NERVE OR BRAIN INJURY MAY APPEAR AT ANY TIME WITHIN THREE WEEKS FOLLOWING AN ACUTE EXPOSURE. AMONG PERMANENT SEQUELAE ARE NEUROPATHIES, VARIOUS MOTOR AND MENTAL DEFECTS, SOME OF WHICH MIMIC MULTIPLE SCLEROSIS OR **PARKINSONISM**, AND DEATH. **PEER REVIEWED** [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology ofCommercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. III-98]

Toxicity

Human Toxicity Excerpt (HTXE):
Rapidly fatal cases of **carbon monoxide** poisoning are characterized by congestion and hemorrhages in all organs. In longer-term,eventually fatal cases, the hypoxic lesions observed are related to the duration of posthypoxic unconsciousness. ... The maximal period of **carbon monoxide** induced posthypoxic unconsciousness compatible with complete neurological recovery is 21 hr in patients under 48 years of age and 11 hours in older patients. Complete recovery of mental functon was not observed when the **carbon monoxide** induced unconsciousness exceeded 15 hours in the older or 64 hours in the younger group. **PEER REVIEWED** [Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990. 1620]

Toxicity

Human Toxicity Excerpt (HTXE):
THE FETUS MAY BE EXTREMELY SUSCEPTIBLE TO EFFECTS OF **CARBON MONOXIDE**, AND THE GAS READILY CROSSES THE PLACENTA. INFANTS BORN TOWOMEN WHO HAVE SURVIVED SHORT TERM EXPOSURE TO A HIGH CONCENTRATION OF THE GAS WHILE PREGNANT OFTEN DISPLAY NEUROLOGICAL SEQUELAE, AND THERE MAY BE GROSS DAMAGE TO THE BRAIN. **PEER REVIEWED** [Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990. 1620]

Toxicity

Human Toxicity Excerpt (HTXE):
Carbon monoxide at levels encountered in tobacco smoke has beensuspected to impair night-time vision. In rats, chronic prenatal exposure to similar concn has been shown to affect visual evoked cortical potentials. **PEER REVIEWED** [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 183]

Toxicity

Human Toxicity Excerpt (HTXE):
A **CARBON MONOXIDE**-INTOXICATED PATIENT DEVELOPED INCR PERMEABILITY-TYPE PULMONARY EDEMA DEMONSTRATED BY A NORMAL CAPILLARY WEDGEPRESSURE AND PRODUCTION OF PROTEIN-RICH EDEMA FLUID. **PEER REVIEWED** [FEIN A ET AL; CHEST 78 (5): 726 (1980)]

Toxicity

Human Toxicity Excerpt (HTXE):
PATIENT WITH POSSIBLE RESIDUAL NEUROLOGIC EFFECTS FROM **CARBON MONOXIDE** AND RETROSPECTIVE STUDY OF PEDIATRIC PATIENTS WITH ACUTEDIAGNOSIS OF **CARBON MONOXIDE** POISONING ARE PRESENTED. EVIDENCE FOR CONCLUSION THAT **CARBON MONOXIDE** CAN PRODUCE RESIDUAL NEUROLOGICAL INJURY IS INCLUDED. **PEER REVIEWED** [BINDER JW, ROBERTS RJ; CLIN TOXICOL 16 (3): 287 (1980)]

Toxicity

Human Toxicity Excerpt (HTXE):
The tissues most affected are those most sensitive to oxygen deprivation, such as the brain and the heart, and the lesions are predominantly hemorrhagic. The severe headache following exposure to **carbon monoxide** is believed to be caused by cerebral edema and increased intracranial pressure resulting from excessive transudation across hypoxic capillaries. **PEER REVIEWED** [Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990. 1619]

Toxicity

Human Toxicity Excerpt (HTXE):

The effects of **carbon monoxide** induced acute elevation of carboxyhemoglobin concentrations on resting and exercise-induced ventricular arrhythmias were evaluated in 10 patients who had ischemic heart disease and in whom no ectopy during baseline monitoring was noted. Patients were exposed to air, 100 ppm **carbon monoxide,** or 200 ppm **carbon monoxide** on successive days in a randomized, double-blind, cross-over fashion. After exposure to 100 and 200 ppm **carbon monoxide,** venous carboxyhemoglobin levels averaged4% and 6%, respectively. Symptom-limited supine exercise was performed after exposure. Eight of the 10 patients had evidence ofexercise-induced ischemia, either angina, 1.0 mm ST depression,or abnormal ejection fraction response, during 1 or more exposure days. Ambulatory electrocardiograms were obtained on each dayand analyzed for arrhythmia frequency and severity. On air and **carbon monoxide** exposure days, each patient had only 0-1 ventricular premature beat/hr in the 2 hr prior to exposure, during theexposure period, during the subsequent exercise test, and in the 5 hr following exercise. **PEER REVIEWED** [Hinderliter AL et al; Arch Environ Health 44 (2): 89-93 (1989)]

Toxicity

Human Toxicity Excerpt (HTXE):
Correlation between carboxyhemoglobin as determined by venous sample and arterial blood pH were studied retrospectively in 49 cases of **carbon monoxide** intoxication. Three cases of smoke inhalation were later excluded. The only therapeutic intervention relating to acidosis or ventilatory status was 100% oxygen administration. The range of carboxyhemoglobin levels was 10 to 64%. Of 18 arterial blood gas samples (pH = 7.37 to 7.54 with a mean of 7.43 + or - 0.04, none showed a correlation between carboxyhemoglobin level and pH. A review of records from 104 additional cases of **carbon monoxide** poisoning showed no significant correlationbetween these parameters. **PEER REVIEWED** [Lebby TI et al; Vet Hum Toxicol 31 (2): 138-40 (1989)]

Toxicity

Human Toxicity Excerpt (HTXE):
A prospective study of the association between **carbon monoxide** poisoning and rhabdomyolysis (myonecrosis) was studied prospectively by obtaining serum creatinine levels on 65 patients (20 to 1315 IU/l) who presented with **carbon monoxide** levels greater than 5.0% (range, 5 to 63.9%). No statistically significant correlation by linear regression analysis between **carbon monoxide** leveland creatinine level was found in these patients. The 4 patients who complained of muscle weakness did not have elevated serum creatinine levels. **PEER REVIEWED** [Shapiro AB et al; Vet Hum Toxicol 31 (2): 136-7 (1989)]

Toxicity

Human Toxicity Excerpt (HTXE):
The simple and interactive effects of **carbon monoxide** exposure and prior physical work on cognitive performance were evaluated

in 16 subjects (healthy males aged 18-29 yr) in 2 hot (WBGT = 30deg C) environments. Three levels of carboxyhemoglobin (0, 7, and 10%) and three workloads (rest, 35% and 60% of a maximum exercise test) were crossed resulting in nine repeated measured conditions per subject. A bolus + ambient air maintenance technique was used to achieve the targeted carboxyhemoglobin levels. Following administration of **carbon monoxide** by bolus, subjects eitherexercised or rested for 50 min, then performed five cognitive tasks: Manikin spatial processing, Sternberg memory, Stroop word color, visual search, and visual tracking, with and without a secondary mathematics task. The only cognitive impairment associated with an elevated carboxyhemoglobin was seen in performance ofthe second of two sequentially presented Stroop test versions using the same stimuli but with competing instructions. Heat exposure per se had no significant effects on cognitive performance based on comparisons with other subjects who underwent the same protocol in a thermoneutral environment. Elevated carboxyhemoglobin was associated with greater reporting of exertion and eye, ear, nose and throat symptoms during heavy exercise concomitant with greater minute ventilation and heart rate. Except for the latter, these effects were not seen in thermoneutral conditions. **PEER REVIEWED** [Bunnell DE, Horvath SM; Aviat Space Environ Med 60 (5): 428-32(1989)]

Toxicity

Human Toxicity Excerpt (HTXE):
/**Carbon monoxide**/ exposure is actually more dangerous for the pregnant woman, who produces nearly twice as much carbon monoxideendogenously each day, and particularly for the pregnant smoker. The increased minute ventilation of gestation also tends to enhance the severity of exposure. **Carbon monoxide** diffuses readilyacross placental membranes or uses carrier-mediated facilitate transfer. While the mother is treated and recovers, the infant may show neurologic or behavioral effects of the prenatal exposure. Fetal CNS damage following nonfatal maternal exposures has been seen in humans and reproduced in animals. **PEER REVIEWED** [Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990. 427]

Toxicity

Human Toxicity Excerpt (HTXE):
The threshold time or **carbon monoxide** content for fetal damage is not known. Normal infant outcome has been reported after maternal coal furnace and smoking exposure produced **carbon monoxide** concentrations of at least 24.5% over a number of hours prior to8 weeks' gestation. The infant was of low birth weight (1950 g at 38 weeks' gestation), but normal development through 6 monthsof age at the time of the report was found. **PEER REVIEWED** [Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990. 427]

Toxicity

Human Toxicity Excerpt (HTXE):
Acute **carbon monoxide** poisoning can cause myocardial injury or aggravate underlying vascular disease. High level chronic exposures (carboxyhemoglobin 20-30%) have been reported to produce a severalfold increase in the incidence of coronary artery disease in tatami may makers in Northern Japan. These workers heated their buildings with charcoal braziers while tightly sealing windows and doors to conserve heat during cold winter weather. **PEER REVIEWED** [Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 170]

Toxicity

Human Toxicity Excerpt (HTXE):
Peripheral neuropathy following **carbon monoxide** intoxication has been reported infrequently and appears to occur only after severe acute exposure. The peripheral neuropathy seen in these cases is associated with demyelination with axonal preservation. Symmetric distal motor weakness and numbness are characteristic findings in case reports. One patient manifested characteristic findings of bilateral ulnar nerve lesions. Some impairment in perceptual discrimination has been associated with long-term exposureto low levels of **carbon monoxide**. **PEER REVIEWED** [Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 565]

Toxicity

Human Toxicity Excerpt (HTXE):
Severe **carbon monoxide** poisoning produces anatomic changes (eg,cerebral edema, hemorrhagic focal necrosis, venodilation, petechiae, perivascular infarct). Bilateral necrosis of the globus pallidus is the characteristic lesion of **carbon monoxide** toxicity.Other vulnerable areas of the cerebral gray matter include the substantia nigra, hippocampus, cerebral cortex, and cerebellum. These histopathological changes are indistinguishable from othercauses such as hypoxia, cardiorespiratory arrest, hypoglycemia,and cyanide poisoning. Rarely, a postanoxic demyelination occurs that follows an initial recovery and progresses to irritability, confusion, coma and death. A 'moth-eaten' appearance characterizes this anoxic leukoencephalopathy in which most of the damage appears in the gray matter of the cerebral cortex, pallidum, thalamus, and cerebellar cortex. **PEER REVIEWED** [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 823]

Toxicity

Human Toxicity Excerpt (HTXE):
Neurologic sequelae include visual loss, dementia, retardation,constructional apraxia, temporospacial disorientation, memory

loss, dysphasia, personality changes, concentration deficits, andfrank psychosis. **Parkinson**'s disease does occur after acute **carbon monoxide** exposures but is very rare. After initial recovery from **carbon monoxide** exposure patients may develop neurologic symptoms (apathy, mutism, amnesia, urinary incontinence, headache,irritability, personality changes, confusion, memory loss, visual changes) within 2 to 4 weeks of exposure. **PEER REVIEWED** [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 824]

Toxicity

Human Toxicity Excerpt (HTXE):
Retinal venous engorgement and peripupillary hemorrhage occur occasionally in both acute and subacute **carbon monoxide** exposures. Their presence should alert the physician to the possibility of **carbon monoxide** poisoning. In one series of 12 poisonings, allpatients exposed to **carbon monoxide** over 12 hours had hemorrhages in the nerve fiber layer of the retina. **Carbon monoxide** decreases light sensitivity and dark adaptation. Cochlear and brain stem hypoxia leads to a central hearing loss and vestibular dysfunction (nausea, vomiting, vertigo), with vestibular symptoms usually more prominent than auditory loss. **PEER REVIEWED** [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 824]

Toxicity

Human Toxicity Excerpt (HTXE):
Several cases of hemolytic anemia have been reported after severe **carbon monoxide** poisoning. Thrombocytopenic purpura with respiratory dysfunction occurred in a patient who had a 20% carboxyhemoglobin level 12 hours post-exposure. **PEER REVIEWED** [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 825]

Toxicity

Human Toxicity Excerpt (HTXE):
A crew of workers in the Holland Tunnel worked 2 hours in an average tunnel concn of 70 ppm **carbon monoxide**, alternating with 2hours out of the tunnel, for 8 hour swing shifts. These workershad an average of 5% carboxyhemoglobin with no one above 10%. The average exposure was approximately 35 ppm, and no symptoms oradverse health effects were observed. **PEER REVIEWED** [American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH,1991. 228]

Toxicity

Human Toxicity Excerpt (HTXE):
... A retrospective study of 1212 tunnel officers exposed to **carbon monoxide**, resulting in less than 5% carboxyhemoglobin, werefound to have a significantly elevated risk of dying from arteriosclerotic heart disease. **PEER REVIEWED** [American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH,1991. 229]

Toxicity

Human Toxicity Excerpt (HTXE):
Two workers with pre-existing coronary artery disease died after exposure to **carbon monoxide** sufficient to produce approximately 25% carboxyhemoglobin. This level could be reached after exposure to approximately 2000 ppm **carbon monoxide** for 15 minutes of light work. **PEER REVIEWED** [American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH,1991. 229]

Toxicity

Human Toxicity Excerpt (HTXE):
A study was made to determine the type, incidence, and timing of complications that occur in patients who have a **carbon monoxide** exposure serious enough to require hyperbaric oxygen therapy. Complication data were retrospectively collected from ten year period for 297 consecutive **carbon monoxide** poisoned emergency department patients who received hyperbaric oxygen therapy. Hyperbaric oxygen therapy was indicated for 41% of the patients becauseof an elevated carboxyhemoglobin level alone. Central nervous system dysfunction, including loss of consciousness and/or cardiovascular dysfunction, was the criteria for hyperbaric oxygen therapy in 59% of patients regardless of their carboxyhemoglobin level. The mean peak carboxyhemoglobin level was 38 mg%, with 88% of patients having a peak carboxyhemoglobin level greater than 25 mg%. The mortality rate was 6% in this case series. Cardiac arrest occurred in 8% of patients: all experienced their first arrest prior to hyperbaric oxygen therapy. The 3% of patients who sustained an isolated respiratory arrest and those who had a myocardial infarction did so prior to hyperbaric oxygen therapy. **PEER REVIEWED** [Sloan EP et al; Ann Emerg Med 18 (6): 629-34 (1989)]

Toxicity

Human Toxicity Excerpt (HTXE):
This paper reports a fetal death due to accidental nonlethal maternal **carbon monoxide** intoxication in which both maternal and fetal carboxyhemoglobin concentrations were obtained. The corrected

carboxyhemoglobin concentration was 61% at the time of death in utero, while the maternal carboxyhemoglobin was measured at 7% after one hour of supplemental oxygen. The mechanisms of fetaldeath were reviewed and it was emphasized the different **carbon monoxide** kinetics in the fetal circulation. **PEER REVIEWED** [Farrow JR et al; J Forensic Sci 35 (6): 1448-52 (1990)]

Toxicity

Human Toxicity Excerpt (HTXE):

The results of the first prospective, multicenter study of acute **carbon monoxide** poisoning in pregnancy were collected and followed. We collected and followed cases of **carbon monoxide** poisoning occurring during pregnancy between December 1985 and March 1989. The sources of **carbon monoxide** were malfunctioning furnaces (n = 16), hot water heaters (n = 7), car fumes In = 63, and methylene chloride inhalation (n = 3). Pregnancy outcome was adversely affected in 3 of 5 pregnancies with severe toxicity; two stillbirths, and one cerebral palsy with tomographic findings consistent with ischemic damage. All adverse outcome occurred in casestreated with high flow oxygen, whereas the 2 cases of severe toxicity with normal outcomes followed hyperbaric oxygen therapy. All 31 babies exposed in utero to mild or moderate **carbon monoxide** poisoning exhibited normal physical and neurobehavioral development. Severe maternal **carbon monoxide** toxicity was associated with significantly more adverse fetal cases when compared to mild maternal toxicity (P less than 0.001). It is concluded that while severe **carbon monoxide** poisoning poses serious short- and long-term fetal risk, mild accidental exposure Is likely to resultin normal fetal outcome. Because fetal accumulation of **carbon monoxide** is higher and its elimination slower than in the maternal circulation, hyperbaric oxygen may decrease fetal hypoxia and improve outcome. **PEER REVIEWED** [Koren G et al; Reprod Toxicol 5 (5): 397-403 (1991)]

Toxicity

Human Toxicity Excerpt (HTXE):

A longitudinal study of one hundred consecutive admissions to the Royal Adelaide Hospital for **carbon monoxide** poisoning was conducted from 1986 to 1989. Twenty-five patients left hospital with persistent symptoms and signs of this poisoning. Five subsequently recovered. Twenty-four other patients, who were well when they left hospital, did not attend for a review one month after discharge. Extensive neuropsychiatric testing at this time showed32% (24 of 76) had obvious sequelae of their exposure. Overall,the frequency of neuropsychiatric sequelae in the patients who only received oxygen at atmospheric pressure was 63 (N = 8) on discharge and 67% (N = 6) on one month follow-up. The frequency of sequelae among those who were given one hyperbaric oxygen treatment only was 46% (N = 24) on discharge and 50% (N = 20) on onemonth

follow-up. In contrast, the frequency of sequelae in patients who had two or more hyperbaric oxygen treatments was only 13% (N = 68) on discharge (P less than 0.005) and 18% (N = 50) onfollow-up (P less than 0.0051 the frequency of sequelae was also significantly greater if hyperbaric oxygen was delayed (P lessthan 0.05). No markers of severe poisoning could be identified. **PEER REVIEWED** [Gorman DF et al; Anaesth Intensive Care 20 (3): P311-6 (1992)]

Toxicity

Human Toxicity Excerpt (HTXE):
Single photon emission computed tomography (SPECT) with technetium-99 (99mTc) hexamethylprophylene amine oxime (HM-PAO) were repeatedly performed in a 55 year old woman with **carbon monoxide** poisoning. The initial brain single photon emission computed tomography 10 days after anoxic insult showed focal hypoperfusion which appeared 20 days prior to the onset of delayed neurologic sequelae, and the findings of follow-up single photon emission computed tomography correlated with the clinical course of **carbon monoxide** poisoning. The possibilities of early hypoperfusion on single photon emission computed tomography of acute **carbon monoxide** poisoning were discussed. **PEER REVIEWED** [Choi IS, Lee MS; Eur Neurol 33 (6): 461-4 (1993)]

Toxicity

Human Toxicity Excerpt (HTXE):
Carbon monoxide is the most frequent cause of immediate fire deaths, and **carbon monoxide** poisoning should be suspected in everyfire victim. **Carbon monoxide** levels at fires may reach 10%, which can raise carboxyhemoglobin levels in active firefighters without respiratory protection to 75% within 1 minute. **PEER REVIEWED** [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 820]

Toxicity

Human Toxicity Excerpt (HTXE):
Two patients, a brother and sister experienced **carbon monoxide** poisoning simultaneously. Both /exhibited/ deficits in frontal lobe/executive functioning along with mild disturbances in memoryand visual spatial information processing. A review of the literature indicates that frontal lobe deficits are commonly found following **carbon monoxide** poisoning along with the /established/ known deficits in memory and visual spatial information processing. **PEER REVIEWED** [Deckel AW; Brain Injury 8 (4): 345-56 (1994)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
...WHEN THE **CARBON MONOXIDE** LEVEL IN THE AIR EXCEEDS 3%, DEATH OCCURS ALMOST AT ONCE. LOWER LEVELS ARE ASSOCIATED WITH VERTIGO,MUSCULAR WEAKNESS, DIFFICULT, RAPID & STERTOROUS RESPIRATION, INTERMITTENT HEART BEAT, LOSS OF POWER OVER SPHINCTERS AND DEATH IN COMA. **PEER REVIEWED** [Humphreys, D.J. Veterinary Toxicology. 3rd ed. London, England: Bailliere Tindell, 1988. 82]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
...EXPOSING /DOGS/...FOR 11 WK, 6 DAYS/WK & 5.5 HR/DAY TO 100 PPM **CARBON MONOXIDE**. ...AS EARLY AS THE SECOND WK THE EKG SHOWED CHANGES WHICH PERSISTED AND AT NECROPSY THERE WERE SIGNS OF DEGENERATION IN INDIVIDUAL MUSCLE FIBERS IN MYOCARDIUM, HEMORRHAGE &NECROSIS. SOME OF THE DOGS HAD SHOWN DISTURBANCE OF GAIT & OF POSTURAL & POSITION REFLEXES, AND AT NECROPSY THERE WERE FOUND HISTOLOGICAL CHANGES IN CORTEX OF THE HEMISPHERES & IN THE GLOBUS PALLIDUS OF THE BRAIN STEM RESEMBLING...THOSE FOUND AFTER ACUTE POISONING BUT SMALLER, MORE SCATTERED & LESS DESTRUCTIVE. **PEER REVIEWED** [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 242]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
...DOGS EXPOSED TO 96 PPM OF **CARBON MONOXIDE** FOR 11 WK SHOWED SIGNIFICANT RISE IN RED CELL COUNT IN 1ST WEEKS, BUT THEN DROP TOTHE ORIGINAL LEVEL OR BELOW. ...INCREASE DUE TO MARROW ACTIVITY/AS/ INCREASED RETICULOCYTES & SOME NORMOBLASTS /WERE FOUND/. ...IN ANIMAL EXPERIMENTS...A RISE IN INTRACRANIAL BLOOD PRESSURE OCCURS UNDER THE INFLUENCE OF **CARBON MONOXIDE**...ATTRIBUTED TO THE INCR CONGESTION AND EDEMA. **PEER REVIEWED** [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 247]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
...EXPOSED RABBITS TO **CARBON MONOXIDE** FOR 8 WK AND FOUND THAT UPTAKE OF CHOLESTEROL IN THE INTIMA OF BLOOD VESSELS WAS CONSIDERABLY ENHANCED. HISTOLOGICALLY INJURIES TO ARTERIAL WALLS CAUSED BY **CARBON MONOXIDE** WERE INDISTINGUISHABLE FROM THOSE CAUSED BY SPONTANEOUS ARTERIOSCLEROSIS. /OTHER/ ...ANIMAL STUDIES INDICATEDTHAT **CARBON MONOXIDE** HAS A DIRECT TOXIC EFFECT ON LUNG TISSUE BY DISRUPTING THE OXIDATIVE METABOLIC CHAIN AND PROFOUNDLY INHIBITS ALL CELLULAR ACTIVITY ESPECIALLY IN HEART AND BRAIN TISSUE WERE THE CELLS HAVE THE GREATEST NEED FOR OXYGEN. **PEER REVIEWED** [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences

Group, Inc., 1974. 252]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
DATA SUGGESTED NO ASSOCIATION BETWEEN PERIODIC **CARBON MONOXIDE** EXPOSURE & DEVELOPMENT OF ATHEROSCLEROSIS IN MONKEYS. **PEER REVIEWED** [BING RJ ET AL; J CLIN PHARMACOL 20 (8-9): 487 (1980)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
PLASMA LEUCINE AMINOPEPTIDASE (LAP) LEVELS AND RESPIRATION RATES OF ISOLATED LIVER MITOCHONDRIA WERE STUDIED IN **CARBON MONOXIDE**-POISONED RATS SAMPLED AT RESP ARREST. INCR IN LAP LEVELS PARALLELED A DECR IN RESP CONTROL RATIO & THE ADP/OXYGEN RATIO. **PEER REVIEWED** [KATSUMATA Y ET AL; FORENSIC SCI INT 16 (2): 119 (1980)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
PREGNANT RATS WERE EXPOSED TO 150 PPM **CARBON MONOXIDE** IN AIR & EXAMINATION OF OFFSPRING SHOWED OFFSPRING WEIGHED LESS @ BIRTH, SHOWED REDUCED GROWTH RATES, & PERFORMED POORLY ON NEGATIVE GEOTAXIS AND HOMING TESTS. **PEER REVIEWED** [FECHTER LD, ANNAU Z; NEUROBEHAV TOXICOL
2 (1): 7 (1980)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
...EXPOSED RABBITS DURING PREGNANCY TO 180 PPM **CARBON MONOXIDE**.PERINATAL DEATH OCCURRED IN 43 OF 123 TREATED OFFSPRING BUT IN ONLY ONE OF A COMPARABLE CONTROL GROUP. THE BIRTH WEIGHT WAS APPROXIMATELY 10 G LESS IN THE TREATED GROUP AND 3 HAD DEFECTS OF THEIR EXTREMITIES. **PEER REVIEWED** [Shepard, T. H. Catalog of Teratogenic Agents. 3rd ed. Baltimore, MD.: Johns Hopkins University Press, 1980. 53]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
The comparative acute toxicity of a branded American cigarette and kreteks (Indonesian cigarettes containing approx 60% tobaccoand 40% ground clove buds) was assessed by exposure of groups of 10 male and 10 female rats to 3 different but equivalent (in terms of total particulate matter) concn of smoke (1.15 to 6.00% v/v) from each type of cigarette. The smoke was delivered "nose only" using a rodent smoking machine within a single 1-hr period, with a total delivery of 30 min smoke and a 15 min air-breathing period between the 2 smoke exposures. The only differences observed were more severe signs of smoke intoxication in the American smoke exposed rats which, at least in part, was attributed to the higher concn of **carbon monoxide. Carbon monoxide** concn in American smoke atmospheres were 2 to 2.5 times higher than that

of kretek smoke (peak concn of 3000 ppm and 1500 ppm, respectively). **PEER REVIEWED** [Clark GC; Arch Toxicol 63 (1): 1-6 (1989)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Arterial blood gases were measured in 52 unanesthetized Sprague-Dawley rats following 6 wk exposure to either room air at ambient altitude (950 m), room air containing 100 ppm carbon monoxideat ambient altitude, room air at 4575 m simulated high altitude, or room air containing 100 ppm **carbon monoxide** at 4575 m simulated high altitude. Pa(CO2) was significantly higher in animals exposed to **carbon monoxide** both at ambient altitude (38.2 vs 34.5 Torr) and simulated high altitude (28.3 vs 23.6 Torr). **PEER REVIEWED** [Davies DG, McGrath JJ; Respir Physiol 75 (2): 193-8 (1989)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Male Fischer 344 rats were exposed continuously for 6 wk to: 100 or 500 ppm **carbon monoxide**; 15,000 feet simulated high altitude; or 100 or 500 ppm **carbon monoxide** at simulated high altitude.Simulated high altitude decr body wt significantly; **carbon monoxide** and **carbon monoxide** /simulated high altitude interaction hadno significant effect on body weight. **Carbon monoxide** and simulated high altitude increased hematocrit ratio significantly; 500ppm **carbon monoxide** increased hematocrit ratio to a greater extent than 100 ppm **carbon monoxide**. There was a significant interaction between 500 ppm **carbon monoxide** and simulated high altitude on hematocrit ratio. The mean electrical axis was shifted to the right by simulated high altitude, and shifted to the left by **carbon monoxide**. The effect was dose dependent, with the greaterleft shift occurring with 500 ppm **carbon monoxide**. **PEER REVIEWED** [Cooper R et al; Physiol Behav 46 (1): 75-9 (1989)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
The effects of **carbon monoxide** were studied in the isolated working rat heart. Hearts removed from male Sprague Dawley rats were perfused via the left atrium with Krebs-Henseleit solution oxygenated with 95% O2/5% CO2 (O2). Heart rate and atrial pressureswere measured by a transducer inserted in the aortic outflow line and connected to a data logger. Aortic flow was determined bycollecting the effluent from the aortic bubble trap in a graduated cylinder. Coronary flow through the pulmonary cannula was collected and measured in a graduated cylinder. After 30 min, the hearts were challenged with solutions containing either **carbon monoxide** (5% CO/90% O2/5% CO2) or nitrogen (N2: 5% N2/90% O2/5% CO2) for 10 min. After recovery in O2, hearts were

challenged with the alternate test solution. **Carbon monoxide** increased coronary flow and coronary flow as a percent of cardiac output 13% and 16% respectively ($P < 0.05$; $P < 0.01$). N2 had no significant effect on either coronary flow parameter. **Carbon monoxide** and N2 had no significant effect on heart rate, cardiac output, oxygen consumption or on aortic flow or pressure. **PEER REVIEWED** [Lin H, McGrath JJ; Physiol Behav 46 (1): 81-4 (1989)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Newborn Sprague Dawley rats were exposed to 500 ppm **carbon monoxide** for up to 32 days of age, at which time the remaining exposed rats and ambient air controls continued development in room air to 200 days of age. In the **carbon monoxide** group, ventricularwt to body wt ratio was 26% greater than controls at 6 days of age, more than double at 15 days, and remained 47% greater at 28days (6 rats per time period). Although absolute myocyte volumes were not different between the two groups at any time period, the **carbon monoxide** group did have greater G myocyte vol relative to body wt during the **carbon monoxide** exposure period. Binucleate myocytes of both ventricles were longer than controls duringthe exposure, but did not have increased width. By 200 days of age, myocytes from left ventricle plus septum of carbon monoxideexposed rats were significantly shorter and **carbon monoxide** exposed rats had more total myocytes than controls (36 million vs 32 million for controls, $p < 0.05$). In this study, cardiomegaly induced by 500 ppm **carbon monoxide** from birth to 32 days of age was primarily to myocyte hypertrophy with myocytes having increased length to width ratios (ie, alterations consistent with a volinduced model). Following removal from **carbon monoxide** exposure, there was regression of both cardiomegaly and myocyte hypertrophy. With increasing time after removal from **carbon monoxide**, myocytes tended to become shorter and smaller compared to age matched controls. This trend was present at 105 days and significantby 200 days of age, resulting in an increased number of myocytes in the myocardium long after removal of rats from **carbon monoxide** exposure. **PEER REVIEWED** [Clubb FJ et al; J Mol Cell Cardiol 21 (9): 945-55 (1989)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Neither the mixed-function oxidase mediated hydroxylation nor the acetylation of aniline was altered by exposure to 7.5% carbonmonoxide/20% O2 for 2.5 hr in isolated perfused rabbit lung. p-Nitroanisole O-demethylation by isolated New Zealand rabbit lungs ventilated with 7.5% **carbon monoxide**/20% O2 for 2.5 hr was significantly decr (approx 37%) in comparison to controls. **PEER REVIEWED** [Trela BA et al; J Toxicol Environ Health 27 (3): 331-40 (1989)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Lungs of male New Zealand rabbits were removed and perfused with

(14)C-4-ipomeanol for 2 hr starting with an initial concn of 0.1 mM. Lungs were ventilated with either air (control) or 7.5% **carbon monoxide**/20% O2. 4-Ipomeanol derived (mixed function oxidase mediated) covalent binding was identical in the control and **carbon monoxide** treatment groups. Lungs perfused with 4-ipomeanoland ventilated with air or 7.5% **carbon monoxide**/20% O2 both displayed alveolar type II cell hyperplasia and alveolar macrophageinfiltration. There was no histological evidence of Clara cell damage in any of the 4-ipomeanol perfused lungs. **PEER REVIEWED** [Trela BA et al; J Toxicol Environ Health 27 (3): 341-50 (1989)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Carbon monoxide, which increases capillary permeability, accelerates plaque formation in animals on atherogenic, high-cholesterol diets. The effect of **carbon monoxide** may actually be due, however, to a lack of oxygen, since atheroma formation is also enhanced in animals subjected to hypoxia. **PEER REVIEWED** [Amdur, M.O., J. Doull, C.D. Klaasen (eds). Casarett and Doull's Toxicology. 4th ed. New York, NY: Pergamon Press, 1991. 450]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Carbon monoxide exposure in rabbits, at 180 ppm exposure for four hours, results in focal intimal damage and edema. This is in the range of **carbon monoxide** exposure that humans might experience from cigarette smoke. **PEER REVIEWED** [Amdur, M.O., J. Doull, C.D. Klaasen (eds). Casarett and Doull's Toxicology. 4th ed. New York, NY: Pergamon Press, 1991. 453]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
One experimental study on the effects of **carbon monoxide** on thenatural history of heart disease in the cynomolgus monkey has been reported. /Animals were/ exposed ... to **carbon monoxide** concentration of 137 mg/cu m (120 ppm) for 24 wk. The average carboxyhemoglobin level of 12.4% resulted in a polycythemia with an increase in hematocrit from 35 to 50%. All animals developed increased P-wave amplitude and T-inversion which suggested nonspecific myocardial stress rather than ischemia. Animals in which an experimental myocardial infarction was produced prior to exposure to **carbon monoxide** had more marked electrocardiographic changes than animals breathing room air. **PEER REVIEWED** [WHO; Environ Health Criteria 13: Carbon Monoxide p.48 (1979)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
When fertilized chicken eggs were continuously exposed to **carbon monoxide** concentration of 747 mg/cu m (650 ppm) for up to 18 days of incubation, the percentage of eggs hatching decreased to 46% and

developmental anomalies of the tibia and metatarsal bones were noted. **PEER REVIEWED** [WHO; Environ Health Criteria 13: Carbon Monoxide p.53 (1979)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Quantitative data on fetal weight of two groups of pregnant rabbits exposed to **carbon monoxide** continually for 30 days /was reported/. Exposure to 90 ppm yielded maternal carboxyhemoglobin concentrations of 9-10% from a control value of 4.5%. Mortality ofthe young rabbits during the following 21 days increased to 25%from a control value of 13%. Doubling the concentration of **carbon monoxide** to 180 ppm resulted in maternal carboxyhemoglobin concentrations of 16-18%, birth weights deceased 20% from 53.7 to 44.7 gm. and neonatal mortality was 35% compared with 1% from the controls. Mortality during the following 21 days was the same value as for the controls, 27%. **PEER REVIEWED** [Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 866]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
The effects of **carbon monoxide** on newborn survival in animals /was studied/. Rats /were exposed/ to mixtures of illuminating gas in air, with inspired **carbon monoxide** concentration of 0.43%. In 22 newborn rats 12-48 hours old exposed to **carbon monoxide**, the average survival times was about 196 minutes, in contrast to an average survival of about 36 minutes in mature animals. **PEER REVIEWED** [Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 866]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
By sequestering intracellular myoglobin of cardiac muscle cellsin the nonfunctioning carboxymyoglobin form **carbon monoxide** blocks myoglobin-facilitated diffusion of oxygen as well as myoglobin-mediated oxidative phosphorylation. ... The hypothesis that the **carbon monoxide** blockade of myoglobin function may be responsible at the cellular level for a component of the cardiotoxicityof **carbon monoxide** observed during exercise /was studied/. Suspensions of isolated rat cardiac myocytes were held in near steady states of oxygen pressure near the intracellular partial pressure of oxygen of the working heart (2 to 5 torr) and near the end-venous partial pressure of oxygen (20 torr). These suspensionswere exposed to **carbon monoxide** at low pressure (0.07 to 70 torr; 90 to 90,000 ppm). The fraction of intracellular carboxymyoglobin determined spectrophotometrically was in good agreement with the fraction predicted from the ratio of **carbon monoxide** partial pressure to

oxygen partial pressure. The effects observed were related to the fraction of intracellular myoglobin bound to **carbon monoxide**. At physiological oxygen pressures no greater than5 torr after sequestration of approximately 50% of the myoglobin steady state oxygen uptake decreased significantly and was significantly less than the respiration of cell groups for which the fraction of carboxymyoglobin was 0% to 40%. When respiration is diminished the rate of aerobic adenosine triphosphate synthesis (oxidative phosphorylation) also decreases. As in the whole heart cytoplasmic adenosine triphosphate concentration in isolatedheart cells is controlled at a constant level by the creatine phosphokinase equilibrium. When adenosine triphosphate utilization is unchanged a sensitive monitor of the decreased adenosine triphosphate synthesis is the ratio of phosphocreatine to adenosine triphosphate. When carboxymyoglobin was at least 40% of the total intracellular myoglobin it was found that the ratio of phosphocreatine to adenosine triphosphate in **carbon monoxide** treated heart cells was significantly lower than that in control cells from the same preparation. Thus, it was concluded that sequestering intracellular myoglobin as carboxymyoglobin significantly decreased the rate of oxidative phosphorylation of isolated cardiacmyocytes. It was estimated that intracellular myoglobin-dependent oxidative phosphorylation will be inhibited when approximately 20% to 40% of the arterial hemoglobin in the whole animal is carboxyhemoglobin. **PEER REVIEWED** [Wittenberg BA, Wittenberg JB; Res Rep Health Eff Inst 62: 1-12(1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
The present experiments investigated alterations of peripheral nervous system activity in male Wistar rats by prenatal exposure(from day 0 to day 20 of pregnancy) to relatively low levels ofcarbon monoxide (75 and 150 ppm). The voltage clamp analysis ofionic currents recorded from sciatic nerve fibers showed that prenatal exposure to **carbon monoxide** produced modifications of sodium current properties. In particular, in 40-day-old rats exposed to **carbon monoxide** (75 and 150 ppm) during gestation the inactivation kinetics of transient sodium current were significantlyslowed. Analysis of the potential dependence of steady-state Nainactivation, h infinity (V) showed that the percentage of the maximum number of activable sodium channels at the normal resting potential (-80 mV) was increased to approximately 85% in **carbon monoxide** exposed rats. Moreover the voltage-current relationship showed a negative shift of sodium equilibrium potential in **carbon monoxide** treated animals. In 270-day-old **carbon monoxide** exposed rats parameters of sodium inactivation were not significantly modified; the reversal potential was still lower with respect to controls.
The results indicate that prenatal exposure to mild **carbon monoxide** concentrations produces reversible changes insodium inactivation kinetics and on irreversible change in sodium equilibrium potential. These alterations could reflect carbonmonoxide influence on the

rate of ion channel development. **PEER REVIEWED** [Carrat'u MR et al; Arch Toxicol 67 (5): 297-301 (1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
In response to acute maternal hypoxia ornithine decarboxylase activity increased significantly in fetal rat brain peaking at 4 hr. This was associated with increased ornithine decarboxylase mRNA and elevated polyamine concentrations. To correlate this response with development we measured ornithine decarboxylase activity in the rat from gestational day E 17 to postnatal day P 10. We also examined to what extent hypoxia induces increased ornithine decarboxylase activity in adult rat brains and whether the response to chronic hypoxia differed from that to acute hypoxia. To test the hypothesis that this increased activity is due to hypoxic hypoxia per se, we subjected pregnant dams to inspired **carbon monoxide** concentrations ranging from 150 to 1000 ppm and assayed ornithine decarboxylase activity in the fetal brain 4 hr later. In the fetus ornithine decarboxylase activity was elevated on E 17 in the cerebrum and cerebellum. It declined gradually toabout one-tenth E 17 levels by E 21 and remained low thereafterexcept for a postnatal elevation in the cerebellum on P 3. In response to 10.5% 02, in the 3-day-old rat, ornithine decarboxylase activity peaked between 2 and 3 hr of hypoxia increasing 3-fold in the hippocampus and 2-fold in cerebellum. Similar increases were seen in the hypoxic adult rat brain. In inspired oxygen dose-response studies exposure of P 3 rat pups to 13.25% 02 for 2.5 hr produced a 1.5-fold increase in ornithine decarboxylase activity; 10.5% 02 produced a 2-3-fold increase while in response to 9% 02 ornithine decarboxylase activity remained at baseline levels. With maternal **carbon monoxide**-hypoxia, ornithine decarboxylase activity increased in the fetal brain at 4 hr, as seen with hypoxic-hypoxia. For example, in hippocampus, ornithine decarboxylase activity doubled at 500 ppm and tripled at 600 ppm. It was concluded: (1) apparently the ability to respond thus is not lost as the animal ages and may represent an important cellular response to acute hypoxia; (2) the increase in hypoxic induced ornithine decarboxylase activity is relative to the already elevated activity seen from E 17 to E 20; a vast reserve for the induction of fetal ornithine decarboxylase activity probably exists and may indicate the importance of this enzyme during this time frame for differentiation and growth promotion: and (3) the **carbon monoxide**-hypoxia studies suggest that some aspects of the cellular responses to **carbon monoxide**- and hypoxic-hypoxia are similar. **PEER REVIEWED** [Packianathan S et al; Developmental Brain Research 76 (1): 131-40 (1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Energy metabolite levels in the brain after a brief exposure tocarbon monoxide were investigated using mice. Male ddY-mice were exposed to **carbon monoxide** in an exposure chamber for 15 minutes and then transferred to room air. Blood was drawn and brain tissue

preparation was conducted at 0 min, 30 min, 4 (hr), 1 day,4 days, or 8 days after exposure. Brain energy charge potentialwas calculated. There was a decrease of spontaneous activities in all mice during **carbon monoxide** exposure, with clonic seizures and death occurring in 33%. Blood carboxyhemoglobin was 63% immediately after exposure; it decreased to 29% 30 min later, and returned to normal in 4 hr. Phosphocreatine, ATP, and energy charge potential levels were lower by 24%, 20%, and 13%, respectively, while adenosine-diphosphate, adenosine-monophosphate, and pyruvate, and pyruvate/lactate ratios were higher by 16%, 216%: 108%, and 209%, respectively. At 4 hr, 1 day, 4 days, and 8 days after exposure, the levels of these metabolites did not differ from those of controls. /It was/ concluded that energy metabolism in the whole brain of mice does not appear to be impaired by acute **carbon monoxide** poisoning. **PEER REVIEWED** [Matsuoka M et al; Research Communications in Chemical Pathology and Pharmacology 81 (1): 15-20 (1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
The kinetics of **carbon monoxide** binding to cytochrome p450 in rat liver microsomes were examined using the flash photolysis technique. Modulation of the kinetics by p450 form-specific effectors such as anti-p450 monoclonal antibodies and substrates was used to elucidate the kinetic behavior of individual p450s within the endoplasmic reticulum.
The problem of attributing a kinetic parameter to a single p450 in the presence of multiple microsomal p450s was overcome with a difference method that employs the difference of the kinetic profiles obtained in the presence and absence of a p450 effector. Applying this approach to study the conformation/dynamics of p450 2B1 in microsomes from phenobarbital-treated rats revealed that the substrate benzphetamine enhances while testosterone inhibits the rate of **carbon monoxide** binding to this p450. Similar experiments with p450 1A1 in microsomes from 3-methylcholanthrene-treated rats showed that the substratebenzo(a)pyrene accelerates **carbon monoxide** binding. These results show that the access channel between solvent and heme in the p450 interior can be altered in a substrate- and p450-dependent manner to either hinder or facilitate **carbon monoxide** diffusion to the heme iron. Analytical difference methods may be employed to characterize the conformation of individual p450s in their native membrane environment in the endoplasmic reticulum. **PEER REVIEWED** [Koley AP et al; Biochemistry 33 (9): 2484-9 (1994)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
A study was conducted to more thoroughly investigate the effects of **carbon monoxide** and cyanide on the electrocardiographic responses in rats. Female Sprague Dawley rats were exposed to 1,500or 2,400 ppm **carbon monoxide** and/or treated with cyanide. **Carbon monoxide** initially induced hyperglycemia and many

fold increases in blood lactate concentration along with rebound increases in blood glucose during recovery. Cyanide produced hyperglycemia,but there was no glucose rebound nor a significant lactate increase. **Carbon monoxide** exposure at the concn used had a major effect in slowing both AV conduction and ventricular repolarizationin the rat. In contrast, cyanide treatment of the rat with 4 mg/kg had little effect on either conduction or repolarization. Falling blood pressure elicited by **carbon monoxide** exposure appeared to be associated with a slowing of ventricular repolarization. **PEER REVIEWED** [Katzman GM, Penney DG; Toxicol Lett 69 (2): 139-53 (1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Wistar female rats were exposed to relatively mild concentrations of **carbon monoxide** (75 and 150 ppm) from day 0 to day 20 of pregnancy. The results show that prenatal exposure to **carbon monoxide** (150 ppm) produced a significant reduction in the minimum frequency of ultrasonic calls emitted by rat pups removed from their nest. Moreover, a significant decrease in the responsiveness(rate of calling) to a challenge dose of diazepam (0.25 mg/kg) was found in male pups exposed to **carbon monoxide** (150 ppm) during gestation. Prenatal **carbon monoxide** (75 and 150 ppm) did not significantly affect locomotor activity or D-amphetamine-inducedhyperactivity in both 14 and 21 day old animals. Furthermore, adult male rats exposed to this chemical (150 ppm) during gestation exhibited significant alterations in the acquisition of an active avoidance task. **carbon monoxide**-induced learning disruptiondoes not seem to be linked to changes in the emotionality of animals. Gestational exposure to **carbon monoxide** induces in rat offspring both short and long term behavioral changes characterized by altered ontogeny of emotional responsiveness to environmental challenges and by learning impairment. **PEER REVIEWED** [Di Giovanni V et al; Brain Res 616 (1-2): 126-31 (1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Adult male rats were exposed to 500 ppm **carbon monoxide** continuously for 30 days, while litter-mate controls remained in room air (AIR). Heart weight-to-body weight ratio and hematocrit were increased significantly. Right ventricle free wall thickness wasincreased significantly as was right to left heart diameter andaverage heart diameter. Cross-sectional areas of the left ventricle free wall, interventricular septum (S) and right ventricle midway between the apex and base were increased significantly. Morphometric analysis of the **carbon monoxide**-exposed and AIR hearts revealed no significant differences in the number of small (27-114 um) or larger (> 114 um) blood vessels in any region; however, there was a trend towards an

increased number of the smaller vessels, both arterioles and venules, in the **carbon monoxide**-exposed rats. The larger arteries in the S and right ventricle were significantly larger in the **carbon monoxide**-exposed rats. There was a significant overall effect of **carbon monoxide** on largerartery diameter across all heart regions, consistent with the appearance of heart radiographs taken. There were no differences in the diameter of the small vessels in any region of the heart between the **carbon monoxide**-exposed and AIR rats. The vessel cross-sectional area of the larger vessels tended to be increased in all regions of the heart. The cross-sectional area of the large arteries in the left ventricle was increased significantly. Arterial wall thickness was decreased significantly in right ventricle and there was a significant overall effect of **carbon monoxide** in decreasing wall thickness and the ratio of wall thickness-to-vessel luminal diameter in these vessels. No vascular pathology was observed. The results suggest changes in coronary vessel architecture during chronic **carbon monoxide**-induced cardiac hypertrophy and are consistent with earlier hemodynamic and morphometric studies of **carbon monoxide** exposed hearts. **PEER REVIEWED** [Penney DG et al; J Appl Toxicol 14 (1): 47-54 (1994)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Carbon monoxide intoxication decr systemic blood pressure and peripheral resistance. ... To assess the role of the skin in thisprocess, the perfusion of hind limb shaven skin in anesthetizedrats /were measured/ during acute moderate **carbon monoxide** intoxication. At a steady blood level of 25% carboxyhemoglobin, the red cell flux was measured as an index of tissue perfusion. ... The mean blood pressure decr by 30% during **carbon monoxide** exposure, but there was no change in mean red blood cell flux of the hind limb skin microvessel bed. ...Rat hind limb perfusion was not affected by acute moderate steady state **carbon monoxide** intoxication. **PEER REVIEWED** [Lee KC et al; Int J Microcirc Clin Exptl 14 (1-2): 62-6 (1994)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
... Studies were conducted to determine the alterations in white blood cells (WBC), red blood cells (RBC), hematocrit (HCT), and hemoglobin (HGB) of maternal and placental blood in protein deprived mice. Mated dams were placed on diets of 16, 8 or 4% protein throughout gestation. The dams were exposed to 0, 125 or 250ppm **carbon monoxide** for 6 hr/day for the first two weeks of pregnancy. ... The amounts of WBC and RBC in the maternal and placental blood were related to **carbon monoxide** exposure levels; the concn of HGB in the maternal blood was also related to **carbon monoxide** exposure levels.

The amounts of WBC, RBC and HGB in the placental blood were related to dietary protein levels. **PEER REVIEWED** [Hill M; Teratol 49 (5): 407 (1994)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
It has been shown, using the method of rat post implantation embryo culture, that the rat conceptus metabolizes the lipoxygenase inhibitor N-hydroxy-N-methyl-7-propoxy-2-naphthalenethamine invitro. The capacity to metabolize /this cmpd/ and accumulate its main metabolites depends on the developmental stage and lengthof exposure. ... To find further evidence for the involvement if cytochrome p450 enzymes in the conceptal metabolism of /this cmpd/, conceptuses preinduced in utero (3-MC or phenobarbital) were exposed to N-hydroxy-N-methyl-7-propoxy-2-naphthalenethamine in vitro and gassed during the second half of the culture periodwith a mixture containing 35% **carbon monoxide**, an inhibitor of cytochrome p450 enzymes. **Carbon monoxide** treatment lead to an inhibition of conceptal metabolism of /the cmpd/ in comparison with that in conceptuses cultured under normal gassing conditions (without **carbon monoxide**). These results strongly suggest the involvement of cytochrome p450 dependent monooxygenases in the conceptal metabolism of N-hydroxy-N-methyl-7-propoxy-2-naphthalenethamine in vitro. **PEER REVIEWED** [Trelouw GD, Bechter R; Toxicol In Vitro 7 (3): 247-58 (1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Hypoglycemia and hyperglycemia were induced in mice by fasting and by injecting with glucose, respectively. These and normally fed (normoglycemic) animals were exposed to 0.5% carbon monoxidefor 10 min. This altered concn of energy metabolites in the brain, including decr in phosphocreatine and incr in creatine and lactate. The only difference between normoglycemic and hypoglycemic mice was lower lactate in the latter. In hyperglycemic mice, phosphocreatine and ATP were better preserved during **carbon monoxide** exposure and lactate was lower than in normoglycemic mice. Blood glucose concn correlated well with glucose but not with lactate in the brain. Thus, moderate hypo or hyperglycemia seems not to exacerbate **carbon monoxide** alterations of brain energy metabolism. **PEER REVIEWED** [Matsuoka M et al; Toxicol Lett 73 (2): 135-43 (1994)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
... Pregnant rats were exposed to **carbon monoxide** daily for a 2hr period throughout gestation. The concn daily for a 2 hr period was between 1,000 to 1,200 ppm. Appropriate pair fed and ad libitum control animals were included to separate the effect of **carbon**

monoxide on fetal growth from maternal underfeeding. Body weights of fetuses exposed to **carbon monoxide** were significantlylower than those of pair fed and ad libitum controls. ... The difference in fetal body weight between pair fed and ad libitum controls was not significant. Litter size was not significantly different among the three groups. The **carbon monoxide** exposed dams had significantly higher hematocrit values than the other two groups. **PEER REVIEWED** [Leichter J; Biochem Arch 9: 267-72 (1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
Wistar female rats were exposed to ... **carbon monoxide** /concentrations/ at 75 or 150 ppm from day 0 to day 20 of pregnancy. Theresults show that splenic macrophage phagocytosis of Candida albicans was significantly decr in 15 and 21 day old male rats exposed to **carbon monoxide** /at 150 ppm/ during pregnancy. ... Splenic macrophage killing was significantly reduced in 15 day old male pups prenatally exposed to 75 and 150 ppm of **carbon monoxide**.Prenatal **carbon monoxide** /at 150 ppm/ significantly decr the splenic macrophage O2 release in both 15 and 21 day old pups. **Carbon monoxide** induced alterations in the immune system were not observed in 60 day old rats. These findings indicate that gestational exposure to ... **carbon monoxide** induces in rat offspring reversible immunological changes characterized by an altered splenic macrophage function. **PEER REVIEWED** [Giustino A et al; Pharmacol Toxicol 73 (5): 274-8 (1993)]

Toxicity

Non-Human Toxicity Excerpt (NTXE):
The involvement of leukocytes in the conversion of xanthinine dehydrogenase to xanthinine oxidase in the brain after **carbon monoxide** poisoning was investigated in rats. Studies were made of male Wistar rats treated with monoclonal antibodies directed against activation dependent, B2 integrin adhesion molecules presenton leukocytes. Rats were exposed to **carbon monoxide** at 1000 ppmfor 40 min followed by 3000 ppm for up 20 min; rats were removed to room air when they lost consciousness. ... Myeloperoxidase activity was incr ten fold in the brain microvessel segments prepared from rats immediately or 90 min after **carbon monoxide** exposure. Leukocytes played a central role in the oxidative stress mediated by **carbon monoxide** poisoning. ... Leukocytes were sequestered in the vasculature. The absence of xanthinine dehydrogenase to xanthinine oxidase and lipid peroxidation in leukopenic rats and in rats treated with anti-CD-18 F(ab')2 fragments indicated that leukocytes were involved in precipitating carbon monoxidemediated biochemical changes. The finds ... were consistent with the theory that **carbon monoxide** mediated brain injury is a type of postischemic reperfusion injury. **PEER REVIEWED** [Thom

SR; Tox Appl Pharm 123 (2): 234-47 (1993)]

Toxicity

Major Populations Threatened (MPT):
MEN WITH CHRONIC **BRONCHITIS** OR ASTHMA RESIST EFFECT OF **CARBON MONOXIDE** VERY BADLY AND COURSE OF **CARBON MONOXIDE** POISONING IS UNFAVORABLY INFLUENCED BY ALCOHOLISM, OBESITY, AND CHRONIC DISEASEOF HEART. CHRONIC VASCULAR DISEASE INCREASES THE DAMAGE DONE TOBASAL GANGLIA. **PEER REVIEWED** [Hamilton, A., and H.
L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences
Group, Inc., 1974. 243]

Toxicity

Major Populations Threatened (MPT):
THE FETUS MAY BE EXTREMELY SUSCEPTIBLE TO EFFECTS OF **CARBON MONOXIDE**, AND THE GAS READILY CROSSES THE PLACENTA. **PEER REVIEWED** [Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990. 1620]

Toxicity

Major Populations Threatened (MPT):
ANEMIC PERSONS ARE MORE SUSCEPTIBLE TO **CARBON MONOXIDE** THAN AREINDIVIDUALS WITH NORMAL AMT OF HEMOGLOBIN. INCR METABOLIC RATE ENHANCES THE SEVERITY OF SYMPTOMS IN **CARBON MONOXIDE** POISONING; THIS IS WHY CHILDREN SUCCUMB EARLIER THAN ADULTS WHEN EXPOSED TOA GIVEN CONCN OF THE GAS. **PEER REVIEWED** [Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990. 1619]

Toxicity

Major Populations Threatened (MPT):
Pregnant women are more susceptible to the effects of **carbon monoxide** exposure. **PEER REVIEWED** [Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]

Toxicity

Major Populations Threatened (MPT):
Smoking cigarettes resulted in higher carboxyhemoglobin levels than exposure to **carbon monoxide** levels present in street air. ... Heavy cigarette smokers may have carboxyhemoglobin levels as high
as 15-17%. **PEER REVIEWED** [WHO; Environ Health Criteria 13: Carbon Monoxide p.74 (1979)]

Toxicity

Major Populations Threatened (MPT):
... On the basis of known effects described, patients with reproducible exercise-induced ischemia appear to be the best established as a sensitive group within the general population that is at increased risk for experiencing health effects of concern (i.e., decreased exercise duration due to exacerbation of cardiovascular symptoms) at ambient or near-ambient **carbon monoxide** concentrations ... Decrements in exercise duration in the healthy population would therefore be of concern mainly to competing athletes, rather than to ordinary people carrying out the common activities of daily life. **QC REVIEWED** [Environmental Health Criteria 213: Carbon Monoxide pp. 17 (1999) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]

Toxicity

Major Populations Threatened (MPT):
... It can be hypothesized, however, from both clinical and theoretical work and from experimental research on laboratoy animals, that certain other groups in the population may be at probable risk from exposure to **carbon monoxide**. Identifiable probable risk groups can be categorized by gender differences; by age (e.g., fetuses, young infants and the elderly); by genetic variations (i.e., hemoglobin abnormalities); by pre-existing diseases, either known or unknown, that already decrease the availablity of oxygen to critical tissues; or by the use of medications, recreational drugs or alterations in environment (e.g., exposure to other air pollutants or to high altitude). Unfortunately, little empirical evidence is currently available by which to specify health effects associated with ambient or near-ambient **carbon monoxide** exposure to these probable risk groups. ... **QC REVIEWED** [Environmental Health Criteria 213: Carbon Monoxide pp. 17-18 (1999) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]

Toxicity

Absorption, Distribution, and Excretion (ADE):
CARBON MONOXIDE IS ELIMINATED THROUGH THE LUNGS WHEN AIR FREE OF **CARBON MONOXIDE** IS INHALED. **PEER REVIEWED** [Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 643]

Toxicity

Absorption, Distribution, and Excretion (ADE):
... /**CARBON MONOXIDE**/ READILY CROSSES PLACENTA. **PEER REVIEWED** [Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990. 1620]

Toxicity

Absorption, Distribution, and Excretion (ADE):
CARBON MONOXIDE IS NOT A CUMULATIVE POISON IN THE USUAL SENSE. CARBOXYHEMOGLOBIN IS FULLY DISSOCIABLE, AND ONCE EXPOSURE HAS BEEN TERMINATED, THE PIGMENT WILL REVERT TO OXYHEMOGLOBIN. LIBERATED **CARBON MONOXIDE** IS ELIMINATED VIA THE LUNGS. **PEER REVIEWED** [Amdur, M.O., J. Doull, C.D. Klaasen (eds). Casarett and Doull's Toxicology. 4th ed. New York, NY: Pergamon Press, 1991. 268]

Toxicity

Absorption, Distribution, and Excretion (ADE):
The absorption of **carbon monoxide** is said not to occur, but itsabsorption followed by oxidation within the epidermis has not been excluded. **PEER REVIEWED** [Hayes, W.J., Jr., E.R. Laws Jr., (eds.). Handbook of PesticideToxicology Volume 1. General Principles. New York, NY: AcademicPress, Inc., 1991. 139]

Toxicity

Absorption, Distribution, and Excretion (ADE):
After continuous exposure to **carbon monoxide** for 49 hr, 50% waseliminated in 30-180 min and 90% within 180-420 min. **PEER REVIEWED** [WHO; Environ Health Criteria 13: Carbon Monoxide p.43 (1979)]

Toxicity

Absorption, Distribution, and Excretion (ADE):
COHb is fully dissociable and, once acute exposure is terminated, the **carbon monoxide** will be excreted via the lungs. Only a very small amount is oxidized to carbon dioxide. **PEER REVIEWED** [Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990. 1620]

Toxicity

Absorption, Distribution, and Excretion (ADE):
The most influential variables in determining carboxyhemoglobinlevels are **carbon monoxide** concn, duration of exposure, and alveolar ventilation. ... The expected blood carboxyhemoglobin values for an average sized adult under conditions of light work for6 to 8 hours at 35 ppm **carbon monoxide** will be approximately 5%. After an exposure of 200 ppm for 15 min, an average adult engaged in heavy work or a smaller adult engaged in light work will have a carboxyhemoglobin level of approximately 5%. **PEER REVIEWED** [American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH,1991. 228]

Toxicity

Absorption, Distribution, and Excretion (ADE):
The relationship between carboxyhemoglobin formation and transient **carbon monoxide** exposure was studied in humans to test the accuracy of the Coburn/Forster/Kane (CFKE) equation for predicting carboxyhemoglobin concn under transient **carbon monoxide** exposure conditions. The study group consisted of 15 male volunteers, mean age 26.5 yr. They were exposed to 6,683 ppm (18)C labeled **carbon monoxide** for 5 min. Radial arterial and antecubital venousblood samples were collected starting 5 sec before exposure andcontinuing up to 10 min after exposure ended, and analyzed for **carbon monoxide**. Minute ventilation and other appropriate pulmonary function parameters were determined .... to calculate the parameters in CFKE equation. The overall mean arterial and venous carboxyhemoglobin concn were 2.08 and 1.39% higher after exposure ended than before exposure began, respectively. The CFKE equation over predicted carboxyhemoglobin concn in venous blood and under predicted carboxyhemoglobin concn in arterial blood. One min after exposure ended, mean arterial carboxyhemoglobin concn began to decr and approached the venous blood carboxyhemoglobin concn in post exposure period ranged from 2.3 to 12.1%, mean 6.2%,regardless of sampling time. The discrepancies were attributed to delays in the appearance of carboxyhemoglobin, approx 1 min in venous blood and 30 sec or less in arterial blood. ... **PEER REVIEWED** [Benignus VA et al; J Appl Phys 76 (4): 1739-45 (1994)]

Toxicity

Metabolism/Metabolites (METB):
Metabolism of the dihalomethanes leads to dehalogenation, and the end product is **carbon monoxide**. ... The **carbon monoxide** appears to arise from a formyl halide intermediate resulting from theloss of one halide atom from the halocarbon. This intermediate as an alternative to losing **carbon monoxide** can covalently bind to cellular protein or lipid. **PEER REVIEWED** [Amdur, M.O., J. Doull, C.D. Klaasen (eds). Casarett and Doull's Toxicology. 4th ed. New York, NY: Pergamon Press, 1991. 692]

Toxicity

Metabolism/Metabolites (METB):
The primary factors that determine the final level of carboxyhemoglobin are: the amount of inspired **carbon monoxide**; minute alveolar ventilation at rest and during exercise; endogenous carbonmonoxide production; blood volume; barometric pressure; and therelative diffusion capability of the lungs. The rate of diffusion from the alveoli and the binding of **carbon monoxide** with the blood hemoglobin are the steps limiting the rate of uptake into the blood. **PEER REVIEWED** [WHO; Environ Health Criteria 13: Carbon Monoxide p.35 (1979)]

Toxicity

Metabolism/Metabolites (METB):
Endogenous production of **carbon monoxide** results from

metabolism of the alpha-methane carbon atom in the protoporphyrin ring /by
hemeoxygenase/ during hemoglobin catabolism and produces a blood carboxyhemoglobin level of 0.4-0.7%. **PEER REVIEWED** [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 820]

Toxicity

Metabolism/Metabolites (METB):
Methylene chloride, a constituent of paint and varnish removers, is converted in vivo to **carbon monoxide**. **PEER REVIEWED** [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 820]

Toxicity

Biological Half-Life (BHL):
THE BIOLOGICAL HALF-LIFE OF **CARBON MONOXIDE** CONCENTRATION IN THE BLOOD OF SEDENTARY ADULTS IS ABOUT 2-5 HOURS. THE ELIMINATION OF **CARBON MONOXIDE** BECOMES SLOWER WITH TIME & THE LOWER THE INITIAL LEVEL OF CARBOXYHEMOGLOBIN, THE SLOWER THE RATE OF EXCRETION. **PEER REVIEWED** [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 396]

Toxicity

Action Mechanism (ACTN):
Carbon monoxide ... reacts /in the blood stream/ with hemoglobin to form carboxyhemoglobin, a form which is incapable of combining with oxygen. Exposure to air containing 0.4% of **carbon monoxide** for 20-30 min results in the conversion of 70% of the hemoglobin in the blood to carboxyhemoglobin. **PEER REVIEWED** [Humphreys, D.J. Veterinary Toxicology. 3rd ed. London, England: Bailliere Tindell, 1988. 81]

Toxicity

Action Mechanism (ACTN):
Carbon monoxide binds tightly to the reduced form of iron in hemoglobin, reducing the delivery of oxygen to tissues. Although this has for many years been thought to be the sole mechanism of toxicity of **carbon monoxide**, there is evidence to suggest that **carbon monoxide** also binds to cytochrome a + a3. **PEER REVIEWED** [Amdur, M.O., J. Doull, C.D. Klaasen (eds). Casarett and Doull's Toxicology. 4th ed. New York, NY: Pergamon Press, 1991. 28]

Toxicity

Action Mechanism (ACTN):
Carbon monoxide and ethylisocyanide act as ligands for

the reduced heme moiety and thus compete with the endogenous ligand, molecular oxygen. These are potent inhibitors of oxidative reactions. **Carbon monoxide** also inhibits p450 mediated reductive reactions. **PEER REVIEWED** [Amdur, M.O., J. Doull, C.D. Klaasen (eds). Casarett and Doull's Toxicology. 4th ed. New York, NY: Pergamon Press, 1991. 113]

Toxicity

Action Mechanism (ACTN):
The affinity of hemoglobin for **carbon monoxide** is between 210 and 300 times greater than its affinity for oxygen, the exact factor depending on pH of the blood and partial pressure of carbon dioxide. ... Furthermore, the presence of carboxyhemoglobin alters the dissociation of oxyhemoglobin so that the remaining oxyhemoglobin is somewhat less efficient in transporting oxygen. **PEER REVIEWED** [Hayes, W.J., Jr., E.R. Laws Jr., (eds.). Handbook of PesticideToxicology Volume 1. General Principles. New York, NY: AcademicPress, Inc., 1991. 172]

Toxicity

Substance Interaction (INTC):
...ADDITION OF CARBON DIOXIDE CAUSED AN INCREASE IN THE RATE OFELIMINATION OF **CARBON MONOXIDE** DUE TO THE INCREASE IN MINUTE-VOLUME IT PRODUCED. **PEER REVIEWED** [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 244]

Toxicity

Substance Interaction (INTC):
...IF RABBITS EXPOSED TO **CARBON MONOXIDE** /FOR 8 WK/ WERE FED CHOLESTEROL, THE ACCUMULATION OF FATS /IN BLOOD VESSELS/ INCREASED3-4 TIMES THAT FOUND IN ANIMALS FED CHOLESTEROL BUT NOT EXPOSEDTO **CARBON MONOXIDE**. **PEER REVIEWED** [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 252]

Toxicity

Substance Interaction (INTC):
Male Fischer 344 rats were exposed continuously for 6 wk to: 100 or 500 ppm **carbon monoxide** (CO); 15,000 feet simulated high altitude; or 100 or 500 ppm CO at simulated high altitude. Simulated high altitude decr body wt significantly; CO and CO/simulatedhigh altitude interaction had no significant effect on body weight. CO and simulated high altitude increased hematocrit ratio significantly; 500 ppm CO increased hematocrit ratio to a greaterextent than 100 ppm CO. There was a significant interaction between 500 ppm CO and simulated high altitude on hematocrit ratio.The mean electrical axis was shifted to the right by

simulated high altitude, and shifted to the left by CO. The effect was dose dependent, with the greater left shift occurring with 500 ppm CO. **PEER REVIEWED** [Cooper R et al; Physiol Behav 46 (1): 75-9 (1989)]

Toxicity

Substance Interaction (INTC):
Eight pairs of male Wistar rats were continuously infused liquid diet and ethanol (8 g/kg/day) or isocaloric dextrose for 4 mo via gastrostomy cannulas. 4 pairs were also continuously exposedto 200 ppm **carbon monoxide** (CO), 24 hr/day, 7 days/wk. Mean ethanol intake (g/kg/day) in the ethanol-CO group (13.3 + or - 0.8)was not significantly different from the mean ethanol intake inthe ethanol-air group (13.4 + or - 0.7). Blood alcohol levels were 277 + or - 64 and 295 + or - 50 mg/dl, respectively. Body wtgain was significantly higher in control rats (both CO control and corn oil control) at 3 mo. Liver damage was followed monthlyby serum alanine aminotransferase and morphologic assessment ofliver biopsy. Serum levels of alanine aminotransferase were significantly higher in the CO-ethanol group compared to other groups at 2, 3 and 4 mo. Electron microscopy revealed a greater degree of cell necrosis in the CO-exposed group which explained its significantly higher alanine aminotransferase activity levels. Both exptl groups (CO-ethanol and air-ethanol) had significantly greater liver damage than controls. Rats showed severe steatosis(75% liver cells infiltrated by fat) in 3 mo. Carboxyhemoglobinlevels were not different in the ethanol fed and control groups. **PEER REVIEWED** [Nanji AA et al; Life Sci 45 (10): 885-90 (1989)]

Toxicity

Substance Interaction (INTC):
Since the hemoglobin of arterial blood is almost completely saturated with oxygen under normal conditions, the breathing of 100% oxygen by a normal person does not significantly increase the amount of oxygen carried in that way, but it does increase the total oxygen content of the arterial blood by about 10% by increasing the physically dissolved oxygen. Because only part of the hemoglobin of a person poisoned by **carbon monoxide** can carry oxygen, the same increase in dissolved oxygen constitutes a greater percentage increase in the total oxygen content of the arterial blood ... about a 20% increase in a person half of whose hemoglobin is rendered useless by **carbon monoxide**. The physically dissolved oxygen is transferred to the tissues with unusual efficiency because of the great difference in its tension in the arterial... blood as compared with the tissues. At the higher partial pressure, oxygen can compete against **carbon monoxide** more effectively for hemoglobin and, by mass action, speed the elimination of the poison. **PEER REVIEWED** [Hayes, W.J., Jr., E.R. Laws Jr., (eds.). Handbook of PesticideToxicology Volume 1. General Principles. New York, NY: AcademicPress, Inc., 1991. 398]

Pharmacology

Therapeutic Uses (THER):
MEDICATION (VET): Euthanasia of dogs and cats can be carried out in a

carbon monoxide chamber, but there are a number of precautions and guidelines for proper use of such chambers. **QC REVIEWED** [Booth, N.H., L.E. McDonald (eds.). Veterinary Pharmacology andTherapeutics. 5th ed. Ames, Iowa: Iowa State University Press, 1982. 1061]

Environmental Impact

Naturally Occurring Sources (NATS):
NATURAL SOURCES SUCH AS ATMOSPHERIC OXIDN OF METHANE, FOREST FIRES, TERPENE
OXIDN & OCEAN (WHERE MICROORGANISMS PRODUCE **CARBON MONOXIDE**) ARE RESPONSIBLE FOR ABOUT 90% OF ATMOSPHERIC **CARBON MONOXIDE**; HUMAN ACTIVITY PRODUCES ABOUT 10%. **PEER REVIEWED** [Gilman, A. G., L. S. Goodman, and A. Gilman. (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 6th ed. New York: Macmillan Publishing Co., Inc. 1980. 1641]

Environmental Impact

Naturally Occurring Sources (NATS):
A small amount of **carbon monoxide** is produced normally in the body. This endogenous **carbon monoxide** is sufficient in amount to maintain a **carbon monoxide** hemoglobin saturation of about 0.4 to 0.7 percent. In some persons with blood disease, such as hemolytic anemia, the **carbon monoxide** saturation may reach 6 percent **PEER REVIEWED** [PATTY. INDUS HYG & TOX 3RD ED VOL2A, 2B, 2C, 1981-1982 p.4117]

Environmental Impact

Artificial Sources (ARTS):
WATER HEATERS ARE A COMMON SOURCE OF **CARBON MONOXIDE**. **PEER REVIEWED** [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 239]

Environmental Impact

Artificial Sources (ARTS):
MOTOR VEHICLES ACCOUNT FOR ABOUT 55 TO 60% OF GLOBAL MAN-MADE EMISSIONS OF **CARBON MONOXIDE**. **PEER REVIEWED** [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 396]

Environmental Impact

Artificial Sources (ARTS):
SINCE MOST...POLYMERIC MATERIALS CONTAIN CARBON, **CARBON MONOXIDE** IS ONE OF THE PRIMARY GASES GENERATED FROM THE HEATING AND BURNING OF THESE MATERIALS /PLASTICS/. **PEER REVIEWED** [Doull, J., C.D. Klaassen, and M. D. Amdur (eds.). Casarett andDoull's Toxicology. 2nd ed. New York: Macmillan Publishing Co.,1980. 551]

Environmental Impact

Artificial Sources (ARTS):
Concentrations as high as 30% have been measured in automobile exhaust gas, although 7% is more common. Pyrolysis of some vinylplastics results in the production of appreciable concentrations of **carbon monoxide**. Natural gas associated with petroleum deposits has no **carbon monoxide** but in processing natural gas (e.g.,cracking), **carbon monoxide** may be produced. As distributed, manufactured gas commonly has a **carbon monoxide** content between 2 and 15% (by volume) **PEER REVIEWED** [GOSSELIN. CTCP 5TH ED 1984 p.III-94]

Environmental Impact

Artificial Sources (ARTS):
A major source of **carbon monoxide** for many people is tobacco smoking. Cigarette smoke contains over 2% **carbon monoxide**, but theaverage concentration in the smoke that reaches the lungs is about 400 ppm **PEER REVIEWED** [PATTY. INDUS HYG & TOX 3RD ED VOL2A, 2B, 2C, 1981-1982 p.4117]

Environmental Impact

Artificial Sources (ARTS):
Portable stoves, formerly called "salamanders," when used to heat buildings under construction may be dangerous sources of **carbon monoxide**. Other sources that may give cause for concern are compressed air for respiratory devices such as supplied-air respirators or "scuba" diving equipment, when supplied from reciprocating compressors, in which **carbon monoxide** may be producedby overheating of lubricating oil **PEER REVIEWED** [PATTY. INDUS HYG & TOX 3RD ED VOL2A, 2B, 2C, 1981-1982 p.4115]

Environmental Impact

Artificial Sources (ARTS):
Estimates have been made of the amounts of **carbon monoxide** (CO)released into the atmosphere as a result of man's activities and influence. Emissions have generally been calculated from the annual consumption of the various source material and the appropriate emission factors. The combustion of petroleum products remains by far the largest source of CO (81.9% in 1979) and the amounts of this gas generated therefrom are rising steadily (from 345.64 Tg in 1965 to 730.21 Tg in 1979). Refuse incineration also makes a sizable contribution but coal combustion is decreasing in importance (from 3.0% in 1965 to 1.4% in 1979). However, although emissions of CO are still increasing (from 468.08 Tg in 1965to 891.83 Tg in 1979), the rate of increase is falling. During the periods 1965-70 and 1970-79 the average annual incr of CO emission

were 5.4% and 3.6% respectively. Global per capita estimates of man-made emissions of CO increased from 140.0 kg in 1965 to 205.72 kg in 1979. **PEER REVIEWED** [Cullis CF, Hirschler MM; Atmos Environ 23 (6): 1195-203 (1989)]

Environmental Impact

Environmental Fate (ENVF):
ATMOSPHERIC FATE: A photochemical model was used to quantify the sensitivity of the tropospheric oxidants ozone (O3) and OH to changes in methane (CH4), **carbon monoxide** (CO), and NO emissionsand to perturbations in climate and stratospheric chemistry. Inmost cases, incr CH4 and CO emissions will suppress OH (neg coefficients) in incr O3 (pos coefficients) except in areas where NO and O3 influenced by pollution are sufficient to incr OH. In most regions, NO, CO, and CH4 emission incr will suppress OH and incr O3, but these trends may be opposed by stratospheric O3 depletion and climate change. **PEER REVIEWED** [Thompson AM, Stewart RW; Atmos Environ 23 (3): 519-32 (1989)]

Environmental Impact

Other Environmental Concentrations (COEV):
Environmental tobacco smoke was analyzed after smoking of research cigarettes by a machine in an experimental chamber 13.6 cu min volume. The ventilation rate was 3.55 air changes per hour. Air removed for sampling added about 0.5 air changes per hour. One cigarette was lit every 30 min and was smoked with a 35 ml puff of 2 sec every minute until extinguished after about 12 min. Mainstream smoke was vented to the outside of the chamber. Additional tests were performed with one cigarette smoked every 15 min and with several commercial cigarette brands. **Carbon monoxide** concentrations averaged 2.48 + or - 0.2 mg/cu m in the first series of 9 tests and 1.79 + or - 0.81 mg/cu m in a similar series.With one cigarette every 15 min the **carbon monoxide** concentrations averaged 4.76 + or - 0.21 mg/cu m. The airborne yield per cigarette was 67 mg of **carbon monoxide**. Concentrations of **carbon monoxide** varied in a saw toothed form with the pattern of smokingone cigarette every 30 min. The ratio of the average maximum tothe minimum concentration was about 3. The average concentration of **carbon monoxide** was about 65 to 70% of the maximum concentration. The ventilation time of **carbon monoxide** corresponded to the predetermined air exchange rate of about 4 per hour. Concentrations of **carbon monoxide** using commercial brands of cigarettes in the chamber and in a tavern setting were similar to those produced by the research cigarettes. **PEER REVIEWED** [Lofroth G et al; Environ Sci Technol 23 (5): 610-4 (1989)]

Environmental Impact

Probable Routes of Human Exposure (RTEX):

...LARGE QUANTITIES OF **CARBON MONOXIDE** GAS RELEASED BY BURNING CHARCOAL CAN RESULT IN SEVERE POISONING OR DEATH. HIBACHIS SHOULD NEVER BE USED AS A SOURCE OF HEAT IN SLEEPING QUARTERS. **PEER REVIEWED**
[Arena, J. M. Poisoning: Toxicology, Symptoms, Treatments. Fourth Edition.
Springfield, Illinois: Charles C. Thomas, Publisher,1979. 240]

Environmental Impact

Probable Routes of Human Exposure (RTEX):
CAR EXHAUST CONTAINS 1 TO 7% **CARBON MONOXIDE**. THIS IS WELL INTO...TOXIC RANGE... **PEER REVIEWED** [Arena, J. M. Poisoning: Toxicology, Symptoms, Treatments. Fourth Edition. Springfield, Illinois: Charles C. Thomas, Publisher,1979. 240]

Environmental Impact

Probable Routes of Human Exposure (RTEX):
Occupational exposure to increased ambient **carbon monoxide** has been a major menace to firefighters, traffic police, coal miners, coke oven and smelter workers, caisson workers, toll both attendants, and transportation mechanics. As commuting distances increase,
workers driving to and from work are exposed to more ambient **carbon monoxide**. **PEER REVIEWED** [Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 540]

Standards and Regulations

Threshold Limit Values (TLV):
BEI (Biological Exposure Index): Carboxyhemoglobin in blood at end of shift
is 3.5% of hemoglobin. **Carbon monoxide** in end exhaled air at end of shift is 20 ppm. The determinant is usually present in a significant amt in biological specimens collected fromsubjects who have not been occupationally exposed. Such background levels are incl in the BEI value. The determinant is nonspecific, since it is observed after exposure to some other chemicals. These nonspecific tests are preferred because they are easy to use and usually offer a better correlation with exposure than specific tests. In such instances, a BEI for a specific, less quantitative biological determinant is recommended as a confirmatory test. (1993) **QC REVIEWED** [American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 99]
ANALYTE: **CARBON MONOXIDE**; MATRIX: AIR; PROCEDURE: INFRARED ABSORPTION SPECTROPHOTOMETRY. **PEER REVIEWED** [U.S. Department of Health, Education Welfare, Public Health Service. Center for
Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed.Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. VI 112-1]

Monitoring and Analysis Methods

Analytic Laboratory Method (ALAB):
ANALYTE: **CARBON MONOXIDE**; MATRIX: AIR; PROCEDURE: COLLECTION INGAS SAMPLING BAG, ELECTROCHEMICAL ANALYSIS. **PEER REVIEWED** [U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed.Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. V4 S340-1]

Monitoring and Analysis Methods

Analytic Laboratory Method (ALAB):
AREAL Method Number IP-3A Determination of **Carbon Monoxide** (CO)or Carbon Dioxide (CO2) in Indoor Air Using Nondispersive Infrared (NDIR). Nondispersive IR Detection Limit = 0.60 mg/m3 **PEER REVIEWED** [USEPA/Atmospheric Research & Exposure Assessment Laboratory (AREAL); Compendium of Methods for the Determination of Air Pollutants in Indoor Air, Engineering Science, One Harrison Park, Suite 305, 401 Harrison Oaks Blvd, Cary, NC 27513 as cited in USEPA;EMMI. Environmental Monitoring Index Database Version 1.02 (1992) EPA/871-B-92-001 (NTIS Document No. PB92-503093)]

Monitoring and Analysis Methods

Analytic Laboratory Method (ALAB):
AREAL Method Number IP-3B Determination of **Carbon Monoxide** (CO)or Carbon Dioxide (CO2) in Indoor Air Using Gas Filter Correlation. GFC Detection Limit = 0.020 ppm **PEER REVIEWED** [USEPA/Atmospheric Research & Exposure Assessment Laboratory (AREAL); Compendium of Methods for the Determination of Air Pollutants in Indoor Air, Engineering Science, One Harrison Park, Suite 305, 401 Harrison Oaks Blvd, Cary, NC 27513 as cited in USEPA;EMMI. Environmental Monitoring Index Database Version 1.02 (1992) EPA/871-B-92-001 (NTIS Document No. PB92-503093)]

Monitoring and Analysis Methods

Analytic Laboratory Method (ALAB):
AREAL Method Number IP-3C Determination of **Carbon Monoxide** (CO)in Indoor Air Using Electrochemical Oxidation. Electrochemical oxidation Detection Limit = 1 ppm **PEER REVIEWED** [USEPA/Atmospheric Research & Exposure Assessment Laboratory (AREAL); Compendium of Methods for the Determination of Air Pollutants in Indoor Air, Engineering Science, One Harrison Park, Suite 305, 401 Harrison Oaks Blvd, Cary, NC 27513 as cited in USEPA;EMMI. Environmental Monitoring Index Database Version 1.02 (1992) EPA/871-B-92-001 (NTIS Document No. PB92-503093)]

Monitoring and Analysis Methods

Analytic Laboratory Method (ALAB):

ASTM Method Number D3162 Standard Test Method for **Carbon Monoxide** in the Atmosphere Continuous Measurement by Nondispersive Infrared Spectrometry. Nondispersive IR Detection Limit = 0.60 mg/m3 **PEER REVIEWED** [ASTM; 1990 Annual Book of ASTM Standards, Sec. 11, Water and Environmental Technology, Vol. 11.03 Atmospheric Analysis; Occupational Health and Safety. ASTM, 1916 Race Street, Philadelphia, PA]

Monitoring and Analysis Methods

Analytic Laboratory Method (ALAB):
ASTM Method Number D3416 Standard Test Method for Total Hydrocarbons, Methane, and **Carbon Monoxide** in the Atmosphere (Gas Chromatographic Method). GCFID Detection Limit not given **PEER REVIEWED** [ASTM; 1990 Annual Book of ASTM Standards, Sec. 11, Water and Environmental Technology, Vol. 11.03 Atmospheric Analysis; Occupational Health and Safety. ASTM, 1916 Race Street, Philadelphia, PA]

Monitoring and Analysis Methods

Analytic Laboratory Method (ALAB):
EMSLR Method Number 2.6 Reference Method for the Determination of **Carbon Monoxide** in the Atmosphere (Nondispersive Infrared Photometry)/ Nondispersive IR Detection Limit 3 ppm **PEER REVIEWED** [USEPA; Quality Assurance Handbook for Air Pollution Measurement Systems., Vol II. Ambient Air Specific Methods, EPA 600/4-77-027a, July 1984]

Monitoring and Analysis Methods

Clinical Laboratory Method (CLAB):
ANALYTE: **CARBON MONOXIDE**; MATRIX: BLOOD; PROCEDURE: GAS CHROMATOGRAPHY. **PEER REVIEWED** [U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed.Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. V1 113-1]

Additional References

Special Report (RPTS):
Anon; J Occupat Med 36 (6): 595-97 (1994). Occupational Medicine Forum. What Are the Potential Delayed Health Effects of High-Level **Carbon Monoxide** Exposure?

Additional References

Special Report (RPTS):
Seger D, Welch L; Annals Emer Med 24 (2): 242-8 (1994). **Carbon Monoxide** Controversies: Neuropsychologic Testing, Mechanisms of Toxicity, and Hyperbaric Oxygen.